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SATURDAY JANUARY 9 1954

TABLE OF CONTENTS

Spontaneous Hyperinsulinism Due to Islet-cell Adenoma K. O. BLACK, M.D., F.R.C.P., R. S. CORBETT, M.Chir., F.R.C.S., J. P. HOSFORD, M.S., F.R.C.S., and J. W. ALDREN TURNER, D.M., F.R.C.P. 55

Invasion of Internal Mammary Lymph Nodes in Carcinoma of the Breast R. S. HANDLEY, M.B., F.R.C.S., and A. C. THACKRAY, M.D. 61

Spinal Epidural Abscess ALLAN HULME, F.R.C.S., and NORMAN M. DOTT, F.R.C.S.Ed., F.R.S.Ed. 64

Low Gametocyte Thresholds of Infection of Anopheles with Plasmodium Falciparum R. C. MUIRHEAD-THOMSON, D.Sc. 68

Rheumatic Heart Disease Complicating Pregnancy M. I. DRURY, M.D., F.R.C.P.I., M. K. O'DRISCOLL, M.B., M.A.O., M.R.C.O.G., M.R.C.P.I., T. D. HANRATTY, M.D., M.A.O., M.R.C.P., M.R.C.P.I., and A. P. BARRY, M.B., M.A.O., F.R.C.O.G. 70

Suxamethonium (Succinylcholine) Chloride and Muscle Pains H. C. CHURCHILL-DAVIDSON, M.D., D.A. 74

Acute Toxic Hypoglycaemia in the Vomiting Sickness of Jamaica D. B. JELLIFFE, M.D., M.R.C.P., D.C.H., D.T.M.&H., and K. L. STUART, M.D., M.R.C.P., D.T.M.&H. 75

Congenital Absence of Both Kidneys PETER E. SYLVESTER, M.R.C.S., L.R.C.P., D.C.H., and DAVID R. HUGHES, M.B., B.Ch., M.R.C.O.G. 77

Use of Unsaturated Fatty Acids in the Eczemas of Childhood JOHN H. S. PETTIT, M.D., M.R.C.P. 79

MEDICAL MEMORANDA

Total Gastrectomy for Haematemesis. JUDSON T. CHESTERMAN, F.R.C.S., F.A.C.S., M.R.C.P. 81

Two Cases of Ovarian Cyst in Childhood. P. T. BRAY, M.B., B.Sc., M.R.C.P., D.C.H., and L. P. THOMAS, M.B., B.Sc., F.R.C.S. 82

BOOK REVIEWS 83

CLINICAL PATHOLOGY

Investigation of Outbreaks of Infection. R. E. O. WILLIAMS, M.D. 91

GENERAL ARTICLES AND NEWS

Medical and Social Problems of the African in Industry. J. H. JACKSON, M.B., B.S. 93

MEDICAL NEW YEAR HONOURS 95

An Improved Undine. L. G. SCOULAR, M.D., D.O.M.S. 96

QUESTIONS AND COMMENTS 107

OBITUARY

Wilfred Shaw, M.D., F.R.C.S., F.R.C.O.G. ..102

A. L. C. Duncan, M.B. 102

Hutchison Burt, M.B., D.P.M. 102

S. W. Innes-Smith, M.M., M.R.C.S. 102

LEADING ARTICLES

Cerebral Arteriography 85

Coronary Disease and Work 86

ANNOTATIONS

Heart Disease and Pregnancy 87

Measurement of Sickness 88

Exchange of Practices 88

A Treatment for Eczema 88

Chlorpromazine for Hypothermia 89

Hospitals and the Public 89

Flexible Endoscopes 90

The New Year Honours 90

CORRESPONDENCE

Radiology and Lumbar Disks. Sir MAX PAGE, F.R.C.S.; D. W. C. NORTHFIELD, F.R.C.S.; H. DAVIES, M.B.; W. HERON, M.B. 97

SUPPLEMENT

Full Contents on First Page of Supplement

Scottish Medical Practices Committee 9

Joint Consultants Committee 10

Metropolitan Counties Branch 10

Correspondence:

Quality and General Practice. BERNARD J. SHAW, F.R.C.S.Ed. 11

CORRESPONDENCE—*cont.*

Ulcerative Colitis. Sir ROBERT HUTCHISON, M.D.; H. A. MCDONALD, F.R.C.S. 98

Malaria in Ex-Servicemen. H. B. WRIGHT, M.D. 98

Infection and Poliomyelitis. J. H. C. CLARKE, M.D. 99

A Cosmetic Amputation. C. R. MCCASH, F.R.C.S.Ed. 99

Distinguishing a Psychopath. C. E. H. TURNER, M.R.C.S. 99

Glycosuria and Hyperglycaemia. W. P. STAMM, M.B. 100

Insulin Zinc Suspensions. GLADYS M. WAUCHOPE, M.D. 100

The Pituitary and Graves's Disease. LAURENCE MARTIN, M.D. 100

Sterilizing Ampoules. D. RECKLESS, M.B. 100

Antibiotics in Bacteriaemia. A. LAWRENCE, M.B. 100

Medresco Hearing-aids. P. G. GRAY, B.Sc. 101

Controlled Hypothermia. E. ZIMMERLI, M.R.C.S. 101

Appendix in the Hernial Sac. J. A. SHEPHERD, F.R.C.S.Ed.; H. B. YOUNG, F.R.C.S.Ed. 101

Royal Medical Benevolent Fund Christmas Gifts. Lord WEBB-JOHNSON, F.R.C.S. ..101

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BRITISH MEDICAL JOURNAL

LONDON SATURDAY JANUARY 9 1954

SPONTANEOUS HYPERINSULINISM DUE TO ISLET-CELL ADENOMA

BY

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Spontaneous hyperinsulinism resulting from a tumour of the islets of Langerhans is not a common condition, and the diagnosis is easily overlooked. Failure in diagnosis usually results in the early death of the patient, while diagnosis followed by operative removal of the tumour cures the majority of patients.

Nicholls (1902) first described an adenoma of the islet cells of the pancreas, but this was an incidental finding at necropsy and no clinical details of the case were recorded. Following the discovery of insulin, Harris (1924) suggested that symptoms might be caused by excess secretion of the hormone, and the first demonstration of an insulin-secreting tumour was by Wilder *et al.* (1927); they explored the pancreas of a doctor, aged 40, who had suffered from attacks of spontaneous hypoglycaemia for eighteen months, and found a carcinoma in the tail of the pancreas with metastases in the liver. The cells of the carcinoma bore a striking resemblance to islet cells, and insulin was extracted from one of the liver metastases.

The first successful operative removal of an insulin-secreting tumour was by Roscoe Graham in 1929 (Howland *et al.*, 1929), who found a small tumour in the body of the pancreas of a woman of 52 who had a seven-years history of attacks of spontaneous hypoglycaemia. The tumour was composed of islet cells, and as it lacked a capsule it was thought possibly to be a carcinoma, but no metastases were found. This lack of a capsule has been a feature of a number of islet-cell tumours subsequently studied, and is not now regarded as an indication of malignancy. Another successful operation was performed at about the same time, for Harvey Cushing (1930), in his Lister Lectures on neurohypophysial mechanisms, mentioned that a small islet-cell adenoma which had caused recurrent attacks of hypoglycaemia had recently been removed in his clinic. Since then the condition has attracted much attention in the United States, no fewer than 38 cases being reported from the Mayo Clinic in twenty years (Lopez-Kruger and Dockerty, 1947), while reviews have been published on both medical (Crain and Thorn, 1949) and surgical aspects of the problem (Howard *et al.*, 1950).

In Great Britain the number of reported cases is comparatively small. Apart from Nicholls's early pathological observation, the first report is that of Barnard (1932), who found an islet-cell adenoma at the post-mortem examination of a patient in whom the diagnosis had been suspected clinically but who had declined further investigation or operation; post-mortem reports have also been published by Cairns and Tanner (1933), Lawrence *et al.* (1942), Webster and Blades (1952), and Cunningham *et al.* (1952). The first successful operative removal of an adenoma in Great Britain seems to be that reported by Fraser *et al.* (1938), and nine other reports of single cases successfully treated by operation have subsequently been published (Rudd and Walton, 1941–2; Rayner and Rogerson, 1943; Haines, 1946; Dickie, 1946; Holmes *et al.*, 1946; Bishton and Malins, 1947; Murray, 1949; Wood, 1951; Smith and Cochran, 1952); and Cohen (1950) has recorded two cases. There has also been a single report of an islet-cell carcinoma with liver metastases (Brearley and Laws, 1950), and one case in which attacks of spontaneous hypoglycaemia were thought to be caused by diffuse hyperplasia of the islet cells without tumour formation (Graham and Oakley, 1950). Richardson and Russell (1952) have reported five cases from the London Hospital; operation was carried out in three of these; in two an islet-cell adenoma was removed with complete relief of symptoms, while in the third patient the tumour was a carcinoma with a metastasis in the liver.

We have had under our care in St. Bartholomew's Hospital in the course of four years three patients with attacks of spontaneous hyperinsulinism, in each of which an islet-cell adenoma has been removed, with a successful result.

Case 1

A male Post Office counter-hand aged 27 was admitted to hospital on August 16, 1947, complaining of fits. The history, obtained from the patient and his wife, started in February, 1946. He then began to have attacks of sweating, trembling, and a feeling of unusual hunger. These occurred in bed in the morning or just before the midday meal. The symptoms were relieved by taking food and usually did not last more than about 10 minutes. At first they occurred infrequently, with symptomless intervals of as long as two or three months, but they grew more frequent, and by October, 1946, were occurring at the rate of one a week. By January, 1947, the attacks had become more severe. They began to occur when he was asleep, and his wife was unable to rouse him. Once he was incontinent, and on another occasion he bit his tongue. Attacks during the day started with blurring of vision, a feeling of dizziness, and

profuse sweating. His arms went useless and stiff, and he lost consciousness. Up to the time of his admission he had been having up to five or six attacks in one week.

There was nothing relevant in the past or family history. He had served in the Middle East during the war and had had sandfly fever. Examination revealed a healthy young man weighing 162 lb. (73.5 kg.). There were no abnormal physical signs, blood pressure was 120/80, and there was no swelling palpable in his abdomen. The urine contained neither albumin nor sugar. The following investigations were done to confirm the diagnosis of organic hyperinsulinism.

Starvation for 18 Hours.—During the last three hours he became drowsy, sweated, and eventually passed into coma. The injection of 5 g. of glucose intravenously resulted in an immediate return to consciousness. Blood sugars during the attack were 45 and 48 mg. per 100 ml.

Glucose-tolerance Test.—After three days on a diet of 350 g. of carbohydrate this test gave the following results. Fasting, 57 mg. per 100 ml. After 50 g. of glucose by mouth: 1 hour, 56 mg.; 2 hours, 125 mg.; 3 hours, 81 mg.; 4 hours, 60 mg.; 5 hours, 58 mg.

Rate of Removal of Intravenous Glucose.—An intravenous drip of glucose solution was begun at the rate of 28 g. per hour, and increased to 33 g. per hour after the third hour. During the first three hours the blood sugar did not rise above 96 mg., and thereafter the highest level reached up to 11 hours was 205 mg. per 100 ml.

The requirements of Whipple's triad were fulfilled in that the attacks came on while fasting, blood sugars during the attack were below 50 mg. per 100 ml., and consciousness was restored by the intravenous injection of glucose.

On September 16 one of us (J. P. H.) explored the pancreas through a transverse epigastric incision. A prolonged search failed to reveal any tumour, and it was decided to do a subtotal resection: about three-quarters of the gland was removed, only the head being left. After operation 24 hours of starvation did not produce any symptoms. A sugar-tolerance curve showed a rise after 50 g. of glucose to 190 mg. per 100 ml., but the blood sugar fell to 50 mg. at the fourth hour. Recovery from the operation was uneventful, and the patient left hospital on November 1.

For two months after operation there were no attacks whatever. Thereafter he had several episodes of sweating and difficulty in waking. By 4½ months after operation he had had three comas. Subsequently there were many minor attacks, which were aborted by taking carbohydrate: on one occasion he bit his tongue.

On readmission to hospital in September, 1948, the nature of the attacks had changed somewhat. The symptomatology was variable, but the sequence in a typical attack was as follows: he would at first continue to walk and talk, but behaved in a childish manner, and on recovery had no memory of his conversation. His face became red, his eyes staring and later wandering. He performed aimless movements with his hands and feet. During this period he would respond to commands. Thereafter his movements became more violent and there was rigidity of the limbs. Untreated attacks culminated in unconsciousness, with eyes wide open and pupils dilated. There was profuse sweating and facial pallor. He sometimes bit his tongue and was incontinent of urine, but the onset was always gradual and he never fell or sustained external injuries.

Blood sugars during attacks were between 40 and 50 mg. per 100 ml. Glucose-tolerance and intravenous glucose-disposal tests were similar to those before operation.

Glucose, by mouth, nasal tube, or intravenously, and adrenaline were effective in relieving the symptoms. Frequent extra feeds between meals and at night were necessary to reduce the number of attacks.

It was clear that a second operation would be necessary, but the patient had become very fat and weighed 215 lb. (97.5 kg.). To diminish the operative risk, efforts were made to reduce his weight. Any attempt to decrease the daily calorie intake was at once defeated by an increase in the amount of glucose needed to treat the hypoglycaemic attacks. Various dietary modifications, ephedrine, and thyroid extract were tried without success. Growth hormone did, however, produce an increase in preprandial blood-sugar levels, a decrease in the amount of carbohydrate necessary to prevent hypoglycaemic attacks, and some reduction of body weight (Black *et al.*, 1952).

On October 11, 1949, J. P. H. again opened the abdomen through a transverse incision, and carefully examined the head of the pancreas. When its posterior surface was exposed by mobilizing the second part of the duodenum a small, firm, rounded nodule was felt in it, and on incising the pancreatic tissue covering it a dark-red encapsulated tumour was exposed and shelled out. The incision in the pancreas was closed with sutures. A drain was put down to the pancreas through a stab wound in the right flank, and through this a temporary pancreatic fistula developed which healed without trouble in a short time.

Pathological Report (Mr. K. C. Richardson).—"The tumour is clearly an islet adenoma composed of cells resembling beta cells. There are a few ducts in the tumour and some islands of abnormal acinar cells. I have not detected any alpha cells. The islets in the fragments of normal pancreas attached to the tumour seem to be normal."

The operation was followed by a mild and transient hyperglycaemia with an insulin requirement of 18 units daily, falling to zero by the end of the third post-operative week. Glucose-tolerance curves have since remained normal, and there has not been any recurrence of hypoglycaemic symptoms. Removal of the tumour was promptly followed by loss of bloated appearance of the face, which had been present before, and a precipitate fall in body weight. Within three months of operation over 3 st. (19 kg.) had been lost, and a more gradual loss continued for a further three months. When last seen in February, 1951, the patient was well and working.

Case 2

A female schoolteacher aged 22 was admitted to St. Bartholomew's Hospital on January 20, 1950, in coma. She had been well till June, 1949, when after a walk of several hours she suddenly felt very tired and unsteady on her legs and was somewhat confused mentally. She managed to get to a café, and after drinking some coffee she recovered in about half an hour. She had three attacks during the next six months, each occurring about the time lunch was due. In one of them she was about to dismiss her class, but found that she could not speak, although she knew what she wanted to say; she then became confused and lost consciousness, the whole attack lasting about an hour. On December 24, after an attack in which she was unconscious for an hour and a half, she was admitted to a hospital. While in this hospital she had four further attacks of loss of consciousness, during which the pupils were dilated and the plantar responses extensor. During two of these attacks she vomited, and on coming round after one to two hours she had no memory of the attack. It was during a further and more severe attack that she was transferred to St. Bartholomew's, having been in coma for about 24 hours. There was no relevant past or family history.

On examination she was in deep coma, pulse 80 and regular, respirations 16, and temperature normal. The pupils were widely dilated and did not react to light, and the fundi were normal. The arms and legs were spastic; tonic neck reflexes could be elicited; the tendon-jerks were abnormally brisk; there was bilateral ankle clonus; and the plantar responses were extensor. The urine contained a trace of ketones but no sugar or albumin.

The blood sugar was 55 mg. per 100 ml.; a ventriculogram carried out to exclude a third-ventricle tumour demonstrated a normal ventricular system; and the electroencephalogram (E.E.G.) was grossly abnormal, with diffuse slow activity, more pronounced on the right than on the left. She was given 15 g. of glucose intravenously and 45 g. six hours later, and a gastric drip was continued for the next 10 days, about 220 g. of glucose together with milk being given through it each 24 hours. Blood sugars, esti-

mated at intervals, varied between 105 and 390 mg. per 100 ml. Recovery from coma was slow: on January 21, 1950, there were periods of weeping and laughing, but she did not respond to commands; on January 23 she understood simple commands and followed people with her eyes; and on the 24th she understood more complicated requests and was able to sip fluids from a spoon. The right plantar response was flexor for the first time, but it was now apparent that she had a left hemiplegia, and the left plantar remained extensor.

A glucose-tolerance test on February 15 gave the following results. Fasting, 86 mg. per 100 ml. After 50 g. of glucose by mouth: ½ hour, 140 mg.; 1 hour, 160 mg.; 1½ hours, 142 mg.; 2 hours, 120 mg.; 3 hours, 69 mg.; 4 hours, 65 mg.; 5 hours, 60 mg.

A series of liver-function tests (van den Bergh, thymol turbidity, and Takata–Ara) were within normal limits; the plasma proteins were 6.75 g. per 100 ml.; and the blood potassium was 19.2 mg. per 100 ml.

The patient remained in hospital till March 19, but no further attacks of loss of consciousness occurred. Her mental state was abnormal, memory was poor, she was emotionally facile, was generally apathetic, and was uncooperative in her physiotherapy. The complete left hemiplegia gradually improved, but on discharge there was still a marked left hemiparesis and she needed a stick when walking. She was seen at intervals as an out-patient, and in the middle of April had a further attack of confusion and difficulty in speaking lasting half an hour. During June and July attacks occurred about once every three weeks, usually in the later afternoon, and lasted from half to two hours; they would start and end fairly suddenly and there was amnesia for the attack. On August 21 she was dull and apathetic at lunch-time and would not eat; she then slumped into a chair, lost consciousness, and was incontinent of urine. This attack lasted four hours, and following it she was readmitted to St. Bartholomew's Hospital, where her blood sugar was found to be 75 mg. per 100 ml. This time the effects of fasting were studied (August 25, 1950).

During the next two weeks several further attacks of hyperinsulinism occurred spontaneously, in one of which there was a generalized tonic-clonic convulsion. Blood sugars in two of these attacks were 42 and 48 mg. per 100 ml.

A glucose-tolerance curve on September 13 gave the following results. Fasting, 66 mg. per 100 ml. After 50 g. of glucose by mouth: 40 minutes, 106 mg.; 1 hour 20 minutes, 116 mg.; 2 hours 40 minutes, 63 mg.; 3½ hours, 61 mg.; 4 hours, 60 mg.; 5 hours, 50 mg.; 6 hours, 46 mg.

Period of Fast	Clinical State	Blood Sugar (mg./100 ml.)	E.E.G.
14 hours	Drowsy, unresponsive to stimuli, dribbling saliva	28	Grossly abnormal. Many high-voltage 1½/2-a-second waves and 4/6-a-second waves
15 „	Unchanged	28	Less abnormal. 1½/2-a-second waves less marked and of low amplitude. Some runs of normal 10 a second activity
16 „	„	35	
17½ „	Still drowsy, but improving. More responsive	50	Deteriorated; similar to the 14-hour record
18½ „	Aware of environment. Answers questions	50	Improved; slow waves less evident. Some fast activity of low voltage
19 „	After an attempt to exercise her, sudden deterioration. Drowsy, unresponsive to stimuli	—	Deteriorated; much slow activity of high voltage
20 „	Drowsy; responds only to strong stimuli	64	As previous record
20½ „	No change clinically	79	
15 ml. of 25% glucose given intravenously			
	Normal within a few minutes	180	Practically normal record

There seemed no doubt that the patient had a functioning islet-cell tumour, and on September 20 one of us (R. S. C.) explored the pancreas, the anaesthetic being thiopentone, gas, oxygen, and curare. For 14 hours she had a gastric drip containing at first 5% and later 15% glucose, and during operation and for 24 hours afterwards 5% glucose intravenously. The abdomen was opened through a right paramedian incision and the pancreas mobilized. A thorough examination of the head was made first, which involved a mobilization of the duodenum by dividing the peritoneum on the lateral side. A gland was dissected out first, adjacent to the common bile duct. Later a nodule was palpated in the substance of the head, and on incision over the posterior surface of the gland a purple-coloured tumour 0.75 cm. in diameter presented, and was removed easily by blunt dissection. The cavity in the gland was obliterated by interrupted catgut sutures and the wound closed. Recovery was uneventful.

Pathological Report (Dr. Cureton).—"A portion of greyish-white tissue measuring 1 by 0.75 cm. and weighing 0.59 g. Sections show this to be an islet-cell adenoma. Specific staining shows that it is almost exclusively composed of beta cells, most of which preserve their granules. One section only shows numerous primitive-looking ducts."

The patient's post-operative recovery was uneventful. She was seen as an out-patient in February and in September, 1951, and on the latter occasion she had returned to work as a schoolteacher and was doing this without difficulty. There had been no further hypoglycaemic attacks, her memory and intellectual ability had improved, and her parents said that she was now co-operative and easy to deal with, whereas before operation she had been uncooperative and irritable. There was still a mild spastic left hemiparesis. In September, 1952, her condition remained the same and there had been no recurrence of hypoglycaemic attacks.

Case 3

A female groom aged 20 was admitted to St. Bartholomew's Hospital on November 1, 1951, complaining of attacks of confusion. Details of the first attack, on July 7, 1951, and of the second, a few weeks later, are vague: they each occurred about three hours after breakfast and consisted of a short period of difficulty in concentration and drowsiness lasting for a few minutes. The third attack occurred on a Sunday morning: the patient did not come down to breakfast, and her mother found her in bed, sweating profusely, not apparently aware of what was said to her, and resisting any efforts to persuade her to get up. The attack passed off in an hour and she was normal again. The fourth attack was on October 3, at the beginning of lunch: she seemed dazed, answered only in monosyllables, put her head into her hands, and burst into tears. She was helped up to bed and was normal within an hour. The fifth and most severe attack was on October 17. After a dance on the previous evening she seemed perfectly well, but on the morning of the 17th was found unconscious in bed. She was seen in consultation by Dr. Philip Buckley, who noted that she was flushed and sweating; her temperature was 96.4° F. (35.8° C.), pulse 90 and regular, and blood pressure 140/95. She was stuporous and resisted examination. The knee-jerks were absent, the ankle jerks feeble, and the plantar responses extensor.

She was transferred to St. John's Hospital, Chelmsford, under Dr. Buckley's care, and at 4 p.m. there was no essential change in her condition. The C.S.F. pressure was 90 mm., there was 1 lymphocyte per c.mm., the protein was 25 mg. per 100 ml., the chlorides were 730 mg. per 100 ml., the sugar content was reduced, and the W.R. was negative. The white blood count was 9,250 per c.mm. (polymorphs 95%, lymphocytes 5%, transitional leucocytes 1%). *X*-ray films of the chest and skull were normal. The blood sugar was 60 mg. per 100 ml., and she was given 20 ml. of 50% glucose intravenously; there was no immediate response, but within 20 minutes she sat up and seemed quite normal except for

some slurring of speech and general bewilderment. Apart from these attacks she had been normal in every way, and had no memory of the attacks.

The patient was a dissimilar twin, and the past history was uneventful except for two minor head injuries due to falls from a horse. There was no family history of epilepsy.

When examined on admission to St. Bartholomew's she was normal mentally, and there were no abnormal signs in the nervous or other systems. Blood pressure was 160/95, and the urine contained neither sugar nor albumin.

As hyperinsulinism seemed the probable diagnosis the crucial test was to induce an attack by fasting: accordingly she had no food on November 4 from 9 a.m. onwards; by 10 a.m. on November 5, after a 25-hours fast, she was drowsy and confused, could give no history, appeared vacant and flushed, and her speech was slurred. She was not, however, sweating noticeably. The pupils were widely dilated but reacted normally to light, and both plantar responses were extensor. At this time the blood sugar was 45 mg. per 100 ml. She was given 50 g. of glucose by mouth and within 20 minutes was fully awake and alert; she seemed normal mentally, her pupils were considerably smaller, and the plantar responses were flexor.

A sugar-tolerance test was carried out after this fast, with the following result. Fasting, 45 mg. per 100 ml. After 50 g. glucose by mouth: 1 hour, 190 mg.; 2 hours, 130 mg.; 3 hours, 89 mg.; 4 hours, 54 mg.; 5 hours, 48 mg.; 6 hours, 46 mg. A barium meal showed no deformity in the duodenum.

An E.E.G. on November 8 (in fasting state—blood sugar 45 mg. per 100 ml.) showed unstable alpha rhythm of very irregular amplitude, with spread into the frontal areas. Excessive generalized slow waves were present in all areas. Overbreathing slowed the alpha rhythm and greatly increased the slower frequencies, which often became paroxysmal and of increased amplitude. After 22 ml. of 33.3% glucose intravenously there was a marked reduction in the slow frequencies, and the alpha rhythm became more steady in amplitude and was reasonably stable.

On November 16 the pancreas was explored by R. S. C. A more extensive search had to be made which involved not only the mobilization of the head of the pancreas, as in Case 2, but also an incision of the peritoneum along the inferior border of the pancreas after entering the lesser sac. It was only after turning up this lower edge of the gland that the tumour was seen embedded in the posterior surface of the tail, lying just above the splenic vein. An enucleoresection was carried out with preservation of the splenic vein. The space left was obliterated with interrupted sutures of catgut as in Case 2 and the pancreas replaced. The wound was closed without drainage. This was an error in technique, for in three weeks a left subphrenic abscess formed in the lesser sac. This was drained through a left lateral incision and the fluid contents showed large quantities of diastase. Following this, recovery was uneventful, and the patient was discharged six weeks later.

Pathological Report (Professor Blacklock).—"The tumour measures 2.5 cm. in its greatest diameter and is 0.5 cm. thick. It is well encapsulated, fragments of the pancreas being still adherent to the capsule. The tumour is rather plum-coloured on the surface, though on section there are paler fleshy areas in it. The tumour weighs 1.85 g. Microscopically the growth consists of masses of small cells resembling the cells of the islet tissue of the pancreas. The tumour is fairly well encapsulated and is a typical islet-cell tumour."

There were no hypoglycaemic attacks after the removal of the islet-cell adenoma, and a glucose-tolerance curve on January 14, 1952, gave a fasting level of 86 mg. per 100 ml., rising to 115 mg. per 100 ml. after 50 g. of glucose and falling to 74 mg. per 100 ml. two hours later.

When seen in May and in November, 1952, she was very well, had had no further hypoglycaemic attacks, and had returned to her work as a groom.

Discussion

Symptoms

The important feature in the early stages, and often throughout the whole course of the illness, is paroxysmal attacks, of which two main types occur. The less serious type was well illustrated by the early attacks in Case 1, and is thought to be due to excess liberation of adrenaline in response to a rapid fall in the blood-sugar level. These attacks consist in sweating, trembling, general weakness, and nervousness, and often palpitations and precordial discomfort without impairment of consciousness. The more serious type of attack is due to a disturbance of cerebral function resulting from the low blood sugar, and these attacks vary greatly in type, not only from patient to patient but in different attacks in the same patient. They may consist of short confusional episodes often associated with automatic behaviour, major epileptic attacks with convulsions, periods of stupor in which bilateral extensor plantar responses may be found, or prolonged coma with, in a severe attack such as occurred in Case 2, signs of decerebrate rigidity. Cerebral attacks were the presenting symptom in Cases 2 and 3, while in Case 1 they began a few months after the onset of attacks, due to excess adrenaline secretion. Attacks of either type tend to occur some hours after a meal and are not uncommon early in the morning, as was well illustrated in Case 3, in which the two severe attacks occurred before breakfast. In general, attacks occur with gradually increasing frequency and severity, though periods of complete freedom may occur as in Case 2, in which after an extremely severe and prolonged attack there was a period of freedom lasting three months.

If the condition is not treated, more permanent changes may develop; in particular there may be a change in personality, with intellectual deterioration and emotional changes. Case 2 presented a curious mental state with poor memory, affective lability, apathy, and a general lack of co-operation, all of which features improved after the removal of the islet-cell adenoma, and within a few weeks of operation her parents thought that her mental condition had returned to normal, and shortly afterwards she resumed her work as a schoolteacher. Comparable mental changes occurred in the patient from the Maudsley Hospital reported by Fraser *et al.* (1938).

Transient focal neurological disturbances such as hemiparesis or aphasia may occur during the attacks of hyperinsulinism, and, more rarely, permanent neurological changes may develop: Case 2 had a complete left hemiplegia following a prolonged hypoglycaemic attack, and, though gradual improvement took place over the course of months, she still had a mild residual hemiparesis: a similar occurrence has been recorded by Crain and Thorn (1949). These rare permanent neurological sequelae are presumably due to actual death of nerve cells resulting from prolonged hypoglycaemia.

Lawrence *et al.* (1942) have studied the cerebral changes in six fatal cases of hypoglycaemia—three diabetics suffering from insulin overdosage, two patients dying during insulin treatment for schizophrenia, and one islet-cell adenoma unsuspected during life—and they found similar changes in all six patients. There was widespread degeneration and necrosis of nerve cells with microglial and macroglial proliferation, the most severe changes being in the cerebral cortex, the caudate nucleus, and putamen, with only slight changes in the cerebellum and brain stem. These changes are very similar to those found in cerebral anoxia and are thought to be due to failure of the normal oxidative processes in the cells from lack of glucose. Although these pathological changes are probably the basis for permanent neurological sequelae, it is difficult to understand why a hemiplegia should occur: one would expect that both hemispheres would be equally affected by prolonged hypoglycaemia, with a resulting double hemiplegia rather than a unilateral hemiplegia, and it is possible that vascular factors are also important.

Lower motor-neurone lesions may also occur as a result of hypoglycaemia and confuse the diagnosis. Silfverskiöld (1946) described two patients with islet-cell adenomas: one developed gross wasting and weakness of the hand muscles, without fibrillation, and weakness of both ankles following a prolonged hypoglycaemic attack; and the other had a bilateral flaccid foot-drop in similar circumstances. Lidz and others (1949) removed an islet-cell adenoma from a patient with severe mental changes, cerebellar ataxia, and extensive muscle-wasting in both legs, without fibrillation: after operation the mental condition and ataxia improved while the muscle-wasting remained unaltered. Tom and Richardson (1951) showed that the cause of a lower motor-neurone lesion of this type was destruction of spinal anterior horn cells occurring during prolonged hypoglycaemia in a patient in whom an islet-cell tumour was found at post-mortem examination. In their case the diagnosis had not been made during life, largely because of the confusing feature of severe localized muscle atrophy in the legs.

Diagnosis

Whipple (1938, 1944) has suggested three criteria for the diagnosis of functioning islet-cell tumours: (1) attacks of nervous or gastro-intestinal disturbance occurring in the fasting state; (2) during the attacks hypoglycaemia with a blood sugar below 50 mg. per 100 ml.; and (3) relief of symptoms immediately by the ingestion of glucose. Whipple's triad is of great value in attacks deliberately induced by a period of fasting as a diagnostic measure, but there may be deviations from it in the attacks which occur spontaneously. In some patients the time relationship of attacks to fasting is by no means obvious, as attacks may occur three hours or so after a meal without any sensation of hunger. More confusing is the fact that the blood sugar may have risen above 50 mg. per 100 ml. while the patient is still unconscious: this was illustrated in Case 3, whose blood sugar was 60 mg. per 100 ml. when she was stuporous and had bilateral extensor plantar responses. Prompt recovery from the attack is usual when glucose is given either by mouth or intravenously, but if the hypoglycaemia has been severe and prolonged this rapid recovery may not occur. Case 3 had been comatose for about 24 hours when she was admitted to St. Bartholomew's and her blood sugar was 55 mg. per 100 ml., but, in spite of intravenous glucose and a gastric drip containing glucose, her recovery was very slow, and it was at least 48 hours before she became conscious.

The most useful confirmatory test is to fast the patient for 12 to 24 hours: if an attack occurs the blood sugar must be estimated and then the effects of oral or intravenous glucose observed. Under these controlled circumstances Whipple's three criteria hold good in the majority of cases. In each of our three patients attacks occurred after 14 hours, and in Case 3 after 24 hours; in each case blood sugars below 50 mg. per 100 ml. were recorded and the attack was rapidly stopped by administration of glucose. We have used this fasting test in a number of other patients whose histories suggested the possibility of hyperinsulinism, most of whom were in fact suffering from epilepsy or hysteria, without an attack being induced and without the blood sugar falling to below 80 mg. per 100 ml.

Differential Diagnosis

Spontaneous hypoglycaemia is known to occur in a variety of conditions. These include organic hyperinsulinism, liver disease, functional hypoglycaemia, certain diseases of the endocrine glands, and a miscellaneous group of which starvation and severe renal glycosuria are examples. None, except the first three, is likely to enter into the differential diagnosis of islet-cell tumour. Hypoglycaemic crises are not a feature of anorexia nervosa, and hypoglycaemic symptoms are absent or unobtrusive. Addison's disease and Simmonds's disease will be recognized by their other clinical manifestations. In practice, then, the problem which confronts the clinician is to distinguish between liver disease, functional hypoglycaemia, and a tumour of the islets of Langerhans.

No difficulty arises with the hypoglycaemia of severe damage to the liver parenchyma with jaundice, but hypoglycaemia occasionally results from minor degrees of liver damage. Conn and others (1938) reported six cases of hypoglycaemia due to an ascending infection of the biliary tract. One of his patients, a man aged 47, had repeated hypoglycaemic crises ending in unconsciousness. These always occurred between 3 and 7 a.m. A biopsy taken at operation showed cholangitis with early biliary cirrhosis. The gall-bladder contained stones and pus, and its removal was followed by complete disappearance of hypoglycaemic attacks. Whipple's triad may fail to distinguish between organic hyperinsulinism and hepatic hypoglycaemia. It is therefore advisable to include radiological examination of the biliary tract and tests of the liver function in the investigation of patients with spontaneous hypoglycaemia.

Difficulty is likely to arise in differentiating organic hyperinsulinism in its early stages from functional hypoglycaemia, which is by far the commonest of all the causes of spontaneous hypoglycaemia. The distinction is an important one, because the treatment of the former is surgical whereas in the latter medical treatment is effective and surgery is to be avoided. It can usually be made with reasonable certainty on clinical grounds. Functional hypoglycaemia is of the stimulative type: the blood sugar is normal even after prolonged fasting, and hypoglycaemic attacks do not occur during the night or before breakfast. They are confined to the daytime and occur two to four hours after meals. The clinical course of organic hyperinsulinism is progressive, the hypoglycaemic crises becoming increasingly severe and frequent, whereas functional hypoglycaemia is not progressive. Undoubtedly the crucial test is the fasting test, which leads to hypoglycaemic symptoms in organic hyperinsulinism but not in functional hypoglycaemia. The glucose-tolerance test is less reliable. The fasting blood sugar is normal in functional hypoglycaemia and the blood sugar falls to subnormal levels two to four hours after the administration of glucose. A sharp rise to 200 mg. per 100 ml. or more immediately after the glucose is characteristic of the hypoglycaemia which sometimes follows operations on the stomach.

Glucose-Tolerance Tests

Glucose-tolerance tests are of less value in the diagnosis of islet-cell tumours than is a fasting test. Very varied results have been recorded in the literature (Crain and Thorn, 1949), but this may be partly due to the fact that they have been carried out under varying conditions of diet. Duncan (1947) has suggested that a standard diet containing 350 g. of carbohydrate in 24 hours should be given for the three days before a six-hour glucose-tolerance test. Under these conditions a patient with a functioning islet-cell tumour usually has a subnormal fasting blood sugar; the highest peak rarely exceeds 120 mg. per 100 ml. and the level falls to subnormal values within two hours, and these low values continue during the third to sixth hours. In our first case a standard diet was given before the glucose-tolerance test: the blood sugar rose to a peak of 125 mg. per 100 ml. and subnormal levels were not reached until the fourth hour. In the other two cases a standard diet was not given, and in fact the tolerance curve in Case 3 was carried out after a 24-hour fast. In this patient the blood-sugar level rose to 190 mg. per 100 ml. at the first hour and did not fall to a subnormal level (54 mg. per 100 ml.) till the fourth hour. In Case 2 glucose-tolerance tests were carried out on two occasions with a seven-months interval between them: the first curve was practically within normal limits except that after three hours the level was 69 mg. per 100 ml. and remained in the sixties at the fourth and fifth hours; the second test fulfilled all Duncan's criteria.

Electroencephalography

It is recognized that marked E.E.G. changes occur during hypoglycaemia: Hoefer *et al.* (1946) studied 11 of Whipple's patients who had functioning islet-cell tumours. The most typical abnormality was high-voltage slow activity occurring

in synchronous bursts all over the head, with considerable improvement in the record after intravenous glucose. He found no clear-cut correlation between the degree of E.E.G. abnormality and the blood-sugar level in the five patients in whom this was studied. In our second patient the E.E.G. was recorded at intervals from the fourteenth to eighteenth hours of a fast, with blood-sugar estimations. The findings of high-voltage slow activity agreed with those of Hoefer *et al.*, and, although from the sixteenth to twentieth hours the blood sugar was rising slowly, there was no progressive improvement in the E.E.G. record or in the clinical state till intravenous glucose was administered, when both the E.E.G. and the clinical condition rapidly returned to normal. In Case 3 when the blood sugar was 45 mg. per 100 ml. the E.E.G. showed generalized slow waves which were greatly increased by overbreathing, and considerable improvement occurred in the record following intravenous glucose. The E.E.G. does not afford any great help in the diagnosis of these patients, but it is perhaps worth stressing that diffuse abnormality in an E.E.G. record of a patient in stupor or coma does not necessarily indicate a primarily intracranial cause for the coma, as both the coma and the abnormal E.E.G. may be the result of disordered brain metabolism from conditions such as hypoglycaemia.

Treatment

The treatment of hyperinsulinism due to an islet-cell adenoma is by surgical removal of the tumour when possible. Once other causes of hypoglycaemia have been excluded and the diagnosis of organic hyperinsulinism has been made, the pancreas should be explored without delay because of the possibility of malignancy, the risk of permanent damage to the central nervous system, and increasing obesity. An intravenous infusion of 5 or 10% glucose solution is set up beforehand and continued throughout the operation. Transient hyperglycaemia may follow operation: it occurred in Case 1 and was easily controlled by soluble insulin, given twice daily.

Medical treatment is notoriously unsuccessful but may be the last resort if operation is refused or if there is a malignant growth with metastases. A predominantly protein-and-fat diet with little carbohydrate, though useful in functional hypoglycaemia, will not prevent the occurrence of severe hypoglycaemic attacks from an islet-cell tumour. A large carbohydrate intake and frequent meals are necessary to prevent attacks. Attempts to destroy the beta cells by alloxan have not been encouraging, and severe toxic effects may result. Extracts of adrenal cortex and of the anterior pituitary have proved disappointing. Growth hormone was tried in Case 1: it produced some elevation of the blood-sugar level, but not enough to be of practical value. It is possible that a combination of adrenocorticotrophin and growth hormone may prove to be more effective.

Surgical Treatment

In all three cases there was a solitary tumour, removal of which brought complete relief of symptoms. A right paramedian incision was used in two cases and a transverse incision in the third, a very adequate exposure of the whole pancreas being obtained in each case.

If the tumour is not seen or felt on any part of the anterior surface of the pancreas, a thorough search must be carried out. The posterior surface of the head is examined by dividing the peritoneum on its lateral side of the duodenum, mobilizing the second part of the duodenum. In Cases 1 and 2 the tumour was felt in this position and was exposed in this way: enucleation was effected after incising the pancreatic tissue over it. An enlarged lymph node was found lying adjacent to the common bile duct in Case 2. The undersurface of the body and tail are examined by making an incision along the inferior border of the pancreas, after entering the lesser sac. In Case 3 the tumour was found on the posterior surface of the tail.

The tumours were enucleated from the pancreas and the cavity obliterated with catgut sutures. It is wise to put a drain down to the area through a stab incision in the right or left loin, to prevent a collection of blood and ferment and to avoid abscess formation. If a pancreatic fistula forms, as in Case 1, it will close spontaneously and the surrounding skin can be prevented from becoming sore by applying suction. In Case 3 the leak produced a subphrenic abscess as a result of not draining.

From the cases reported it seems that these tumours are small (1–2 cm.), red or purple in colour, and firm in consistency compared with ordinary pancreatic tissue. They are often buried in the gland and can occur anywhere from the head to the tail. In Case 1 the search was given up at the first operation and in Case 3 it was almost given up. A lymph node may be mistaken for the tumour on palpation, but the appearance (Case 2) is quite different. No sign of malignancy was found, which from reports is a rare occurrence.

Summary

Three cases of spontaneous hyperinsulinism due to an islet-cell adenoma are described. The removal of the adenoma in each case resulted in relief of symptoms, whereas a resection of three-quarters of the pancreas in one patient had caused only temporary improvement.

The symptomatology is discussed, and it is stressed that permanent neurological damage may occur in a prolonged hypoglycaemic attack.

The crucial diagnostic test is a period of fasting of up to 24 hours. In attacks produced in this way Whipple's diagnostic triad is fulfilled, which is not invariably true in spontaneous attacks.

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Four field medicines issued to British troops during the Crimean War have been added to the Pharmaceutical Society's historical museum. The bottles, labelled "The British Pharmacy, Smyrna," contain powdered rhubarb, milk of sulphur and cream of tartar, calcined magnesia (for indigestion), and ipecacuanha wine (for coughs).

INVASION OF INTERNAL MAMMARY LYMPH NODES IN CARCINOMA OF THE BREAST

BY

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For the past 150 years isolated observers have been calling attention to the internal mammary lymph chain and its importance in the spread of carcinoma of the breast. No great notice has been taken of their words because they have not provided convincing proof. In 1946 it occurred to us that quantitative microscopical proof of the role of the internal mammary chain in malignant disease of the breast could be obtained by biopsy during the course of a radical mastectomy. The surprising results of this simple procedure have from time to time been published (Handley and Thackray, 1947, 1949; Handley, 1950, 1952). It is intended now to bring this published information up to date and to try to discern whither the facts are leading in the realm of treatment.

Anatomy of the Internal Mammary Lymphatic Chain

The internal mammary lymph nodes receive lymph chiefly from the medial side of the breast and from the region of the nipple, but there is considerable overlap in the territories drained by them and by the axillary system. Afferent lymphatics from the breast reach the chain by perforating the intercostal muscles, for the most part where the anterior perforating arteries emerge. The nodes themselves lie posterior to the intercostal muscles, and Stibbe's (1918) diagrams (Figs. 1 and 2) show their general arrangement. They are inconstant both in position and in number, and there exist many very tiny nodes which are recognizable only by the microscope. The chain begins in the sixth intercostal space, where it receives lymph from the diaphragm and liver, and it ends, again inconstantly, in a node which lies behind the sternal head of the sterno-mastoid muscle and which discharges direct into the great veins. Nodes most often occur in the second, first, and third spaces in that order of frequency, and it is to nodes in these spaces that lymph from the breast is mostly discharged.

Technique of Internal Mammary Biopsy

To remove a node for purposes of biopsy is a finicking procedure, but by no means difficult. A 1-in. (2.5-cm.) incision in the intercostal muscles, running from the edge of the sternum, midway between and parallel with the costal cartilages, will reveal extrapleural fat, imbedded in which are the lymph nodes of the chain and the internal mammary vessels; the latter usually lie about ¼ in. (6 mm.) clear of the sternum. To detach lymph nodes requires a nice touch with two pairs of dissecting forceps, particularly as the nodes are often minute; any fatty tissue removed from a plane deep to the intercostal muscles should be sectioned as it often contains a microscopic node. The only peril attending the procedure is laceration of the internal mammary artery, but this accident should be easy to avoid, and has not occurred in the series described here. Tears of the pleura are of no great consequence if they are recognized, and this accident has occurred to us on five occasions without untoward post-operative sequels.

Material

The series on which internal mammary biopsy has been carried out consists of 150 cases. It is as continuous as it has been possible to make it. All patients being treated for the first time by surgery have been subjected to the biopsy. Second primary tumours occurring in the opposite breast, tumours in men, and tumours treated first by radiotherapy have been excluded. Of the 150 patients, 139 have been judged, on clinical grounds, to be operable; in 11 the biopsy was exploratory in patients who were judged inoperable. During the time in which these numbers have been accumulating, approximately 45 additional cases have been seen in which, for one reason or another, but chiefly because of advanced spread, surgery as a primary measure has not been undertaken and no biopsy has been done; it is reasonable to suppose that, had they been included, the overall percentage of invasion of the internal mammary chain would have been higher. An analysis by quadrant, and by the numbers in which axillary metastases were found, does not differ greatly in its distribution from the large published series—for example, Truscott (1947)—and it may therefore be taken that our series is representative in these respects. One of us (R. S. H.) has done all the biopsies and the great bulk of the accompanying surgery. The latter, in the 139 operable cases, has consisted of 117 radical mastectomies, 3 Margottini operations, 3 Urban operations (see below), and 16 extended simple mastectomies. All diagnoses are based on histological evidence, with the exception of the state of the axillary nodes in one of the clinically operable cases and in 8 of the 11 inoperable cases. All these unproved axillary nodes have been reckoned as invaded. In the earlier cases only the second intercostal space was explored.

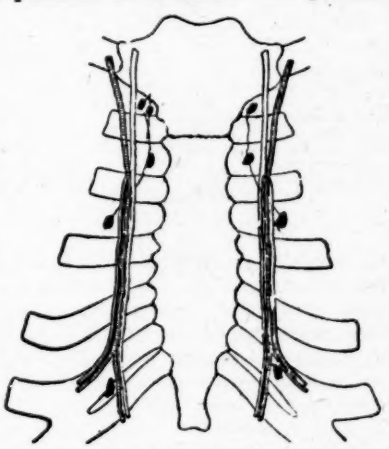

FIG. 1.—The internal mammary blood vessels and chain of lymph nodes seen from within the thorax. (After Stibbe.)

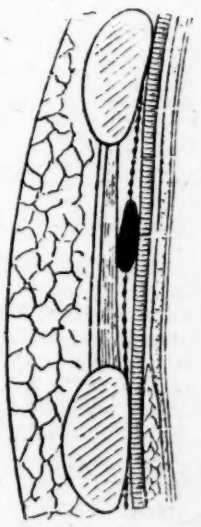

FIG. 2.—Sagittal section of the chest wall showing the pectoralis major to the left, two costal cartilages cut across, and an internal mammary lymph node lying behind the intercostal muscles. (After Stibbe.)

Later more than one space was often explored, and recently the upper three spaces have been explored as a routine. There has been no mortality.

Results

Table I shows that 33% of the primary growths in this series had metastasized to the internal mammary chain at the time of operation. If the 61 growths in the medial half of the breast (with which are included the tumours behind the nipple) are considered, 33 (54%) of them had metastasized to the chain, 6 of them to the chain alone, whereas only 16 of the 89 growths (18%) in the lateral half of the breast had metastasized to the chain, and 2 to the chain alone. Table II shows a further breakdown by quadrant, and it is of particular interest that 16 of the 17 growths in the region of the nipple had metastasized to lymph nodes, in 12 the internal mammary chain being invaded.

TABLE I.—*Lymphatic Spread of Breast Cancer in Relation to Site of Primary Growth*

	Site of Primary Growth		Total
	Inner Half of Breast	Outer Half of Breast	
All nodes free	16	33	49
Axillary nodes only invaded	12	40	52
Internal mammary nodes only invaded	6	2	8
Both axillary and internal mammary nodes invaded	27	14	41
Total No. of cases	61	89	150

TABLE II.—*Lymphatic Spread of Breast Cancer in Relation to Site of Primary Growth, by Quadrant*

	Site in Breast by Quadrants					Total
	Upper Inner	Lower Inner	Central	Upper Outer	Lower Outer	
All nodes free	11	4	1	28	5	49
Axillary nodes only invaded	6	2	4	34	6	52
Internal mammary nodes only invaded	4	0	2	2	0	8
Both axillary and internal mammary nodes invaded	10	7	10	13	1	41
Total	31	13	17	77	12	150

If only the tumours which had already metastasized to the axilla are considered, 41 of the 93 cases (44%) had metastasized to the internal mammary chain. Of the 39 cases in which a tumour in the inner half of the breast had metastasized to the axilla, the internal mammary chain was invaded in 27 (69%). Even with tumours in the outer half of the breast, if the axilla was invaded 14 of the 54 cases (26%) had internal mammary deposits.

An attempt was made to see whether the degree of anatomical invasion of the axilla bore any relation to the frequency of internal mammary deposits. There were 146 cases in which the data enabled a rough estimate to be made of the anatomical degree of axillary involvement, and four degrees, from 0 to 3, were somewhat arbitrarily fixed by the clinical state of the patient, the number of invaded lymph nodes sectioned, and whether or not the apical axillary nodes were involved.

Table III gives the results, and it shows what one might expect—namely, that the greater the degree of axillary involvement the more likely is it that the internal mammary chain will be invaded—but it disposes of the argument that only after the axillary lymphatics are completely choked is the chain invaded.

TABLE III.—*Relation of Degree of Axillary Involvement to Internal Mammary Invasion (146 Cases)*

Extent of Axillary Invasion	No. of Cases	Cases with Internal Mammary Invasion
0 (free)	57	8 (14%)
1 (light)	23	6 (26%)
2 (moderate)	32	12 (37%)
3 (heavy)	34	22 (65%)

To compare the results of different workers in the field of mammary cancer, some index of the extent of the disease in individual cases is needed. A system of staging has therefore been evolved, based for deciding treatment on the clinical findings and for scientific purposes on pathological and radiological evidence. We have staged our cases into three groups according to whether the carcinoma was confined to the breast (stage I), had not spread beyond the limits of the standard radical mastectomy (stage II), or had spread beyond those limits (stage III). We have thus placed a patient with internal mammary deposits in stage III. No other series, however, has been staged in the light of internal mammary biopsy, and it seems that this may account for the very small differences in the results of treatment which many have found between stages II and III. Yet, without knowledge of the state of the internal mammary nodes, a stage III case must often be classified as stage II and occasionally as stage I.

Table IV shows the effect of internal mammary biopsy on staging. It demonstrates the well-known though appalling inaccuracy of clinical staging. The last two columns of the table reflect the effect of the biopsy procedure on the pathological staging. Whereas stage I is not much affected, there is a "landslide" between stages II and III, the 85 stage II cases being reduced by the biopsy findings to a mere 52, and the stage III cases being increased from 8 to 49.

TABLE IV.—*Effect of Internal Mammary Biopsy on Staging*

	Clinical	Pathological	
		Ignoring Internal Mammary Findings	In Light of Internal Mammary Findings
Stage I	79	57	49
" II	63	85	52
" III	8	8	49

In this series 75 patients had their biopsies three or more years ago. The results in terms of three-year survival are shown in Table V. Three-quarters of the patients with metastases only in the axilla are alive, whereas only one-third of those with both axillary and internal mammary metastases are still living.

TABLE V.—*Three-year Survival (75 Cases)*

	Total No. of Cases	No. Alive
All nodes free	24	22 (all well)
Axillary nodes only invaded	24	18 (5 with recurrence)
Internal mammary nodes only invaded	4	4 (all well)
Both internal mammary and axillary nodes invaded	23	8 (3 with recurrence)

The result has been good in those in whom the lymph nodes were not invaded. But one striking and apparently contradictory result is that all the four patients in whom the internal mammary chain alone was invaded are alive and well, a finding which does not accord with the importance which we would give to invasion of the internal mammary chain; it may be that what was intended only as a biopsy was, by lucky chance, an effective therapy in an early internal mammary invasion.

Discussion

It has long been known that carcinoma of the breast may spread by way of the internal mammary chain, but this has been assumed to be a late manifestation of the disease and has not been taken into account in planning the primary treatment. What the present investigation demonstrates is the frequency with which the chain is involved in cases

operated upon as soon as the diagnosis is made, especially when the primary tumour is in the inner part of the breast. About a third of the operable cases have been shown to have deposits in their internal mammary glands, the tumour being therefore beyond the reach of the standard radical mastectomy. Since other workers, stimulated by our original publication, have repeated the investigation, sometimes on larger series than our own and with substantially the same findings, the frequency and importance of internal mammary spread can be taken as satisfactorily demonstrated (Dahl-Iversen, 1951; Gardner *et al.*, 1951; Haagensen, 1952, personal communication; Margottini, 1952; Moguilevsky, 1952, personal communication; Redon and Lacour, 1952; Wangensteen, 1952, personal communication). The discussion will therefore be confined to a short consideration of the effect of this finding on the treatment of the disease.

It has been suggested that, once the internal mammary chain has been invaded, the patient's situation is irremediable, because tumour cells must then have spread beyond therapeutic reach along this or other pathways. Though it is not possible at the present time to disprove this view, only the darkest pessimist would decline the challenge which invasion of the internal mammary chain presents. Halsted, when he introduced radical mastectomy, had never seen a case of carcinoma of the breast cured, and he did not know what the result of his new operation would be. To devise methods for treating the internal mammary deposits is therefore a very proper experiment, but one which it will need some years to evaluate.

Surgical excision and radiotherapy are the only potentially curative methods which exist at present for attacking the internal mammary chain. It is natural that radiotherapy should have been tried first, because until recently wounds of the pleura were regarded by surgeons with dread, and even now no surgeon would wish to add further mutilation to radical mastectomy unless he had compelling reasons for doing so. The first attempt to irradiate the internal mammary chain as a routine was Sampson Handley's (1927) method of burying radium tubes in the intercostal spaces at the time of radical mastectomy. The results were not encouraging, partly perhaps because the intensity of irradiation round a radium needle falls very rapidly and uniform carcinolytic dosage is not therefore achieved along the whole chain, and partly because it is technically difficult to insert radium needles in the very narrow anterior ends of the lower spaces.

In the mistaken belief that surgical excision of the chain was not feasible, we decided in 1947 to treat the chain in our series by deep *x*-ray therapy, and we enlisted Professor B. W. Windeyer's willing co-operation. It is, however, difficult to deliver an adequate dose of irradiation to the chain without damaging adjacent normal structures, and the only evidence we have so far obtained is not particularly reassuring. This evidence is the three-year results in our first 75 patients, quoted already, who were treated by radical mastectomy and, if any lymph node was invaded, by deep *x*-ray therapy; and the results of internal mammary biopsies done on nine cases (not included in the main series) in which radiotherapy was the first line of attack on the primary tumour. Six of these nine cases were regarded as inoperable when first seen, and in five cases carcinoma cells of viable appearance were seen in the post-irradiation biopsy. Three were earlier operable cases, and in all the biopsy was negative. These results have led Professor Windeyer to alter his technique in order to irradiate the chain more intensively, and the results of this change will be awaited with interest.

This evidence is not so satisfactory as to make experimental extensions of the standard radical mastectomy unjustifiable. Margottini and Bucalossi (1948) were the first to add excision of the chain as a routine, which they did by removal of the second and third costal cartilages, thereby gaining access to the upper part of the chain without deliberately entering the pleura. The chief theoretical objection to their procedure is that it is not a monobloc operation. Wangensteen (1950) has described his super-radical mastectomy, which combines a supraclavicular dissection with a median sternotomy and removal of lymph nodes not only in both internal mammary chains but also further inside the chest. He has not yet published his results, but the mortality of this operation seems to be considerable, and it also suffers from the theoretical disadvantage that it is not a monobloc procedure. Urban (1952) has published a technique which appeals to us as the most likely to yield better results, because by a deliberate opening of the pleura he achieves excision of the upper part of the internal mammary chain in one piece with the breast and axillary tissue, an operation which he has done 103 times with one death. All such extensions of surgical treatment, however low their mortality in the hands of their architects, would, if generally adopted, raise the immediate death rate of breast-cancer surgery. Until their value has been proved, there is no reason for those without a prime interest in carcinoma of the breast to abandon accepted methods.

The problem of carcinoma of the breast holds many imponderable factors. We cannot yet assess with much accuracy the malignancy of tumours, and we know almost nothing about host resistance to their spread. Until the biochemistry of tumour growth and host-resistance is better understood we can only grope by mechanical means along therapeutic paths which are dimly indicated by morbid histology and judge by the slow criterion of the end-result whether the technique we follow is better (or worse) than its predecessor.

Summary

Biopsy of the internal mammary lymph chain at operation was carried out in 139 patients with "operable" carcinoma of the breast. In 41 cases (29%) invasion of the chain by carcinoma was found on histological examination. Of a further 11 "inoperable" cases, 8 showed invasion of the chain.

Invasion of the chain was three times as frequent when the primary growth was situated in the inner half of the breast as when it was in the outer half.

Biopsies of the internal mammary chain in patients with primary growths in the inner half of the breast and metastasis in the axillary lymph nodes showed invasion in over two-thirds of the cases.

The internal mammary chain was invaded in eight cases without involvement of the axilla.

The relation of the biopsy procedure to staging and three-year survival is studied.

Some tentative reflections on the therapeutic challenge presented by these findings are offered.

Our thanks are due to Mr. D. H. Patey, Professor R. W. Scarff, and Professor B. W. Windeyer for constructive criticism. Part of the expense of this investigation was defrayed by the British Empire Cancer Campaign.

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SPINAL EPIDURAL ABSCESS

BY

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Infection of the spinal epidural fatty areolar tissue by pyogenic organisms is generally regarded as a rare condition. Although a well-recognized clinical entity, it has received little attention in British medical literature. In contrast, that of the United States contains a number of excellent reviews of the subject, notably by Dandy (1926), Gasul and Jaffe (1935), Browder and Meyers (1937, 1941), Rankin and Flothow (1946), Huesner (1948).

In 1926 Dandy found only 25 cases in the literature. Rankin and Flothow were able to review 225 cases in 1946, and two years later Huesner reported a further 20 cases.

This communication is based upon a series of 25 cases of spinal epidural suppuration, 19 of which have been treated in the department of surgical neurology, Edinburgh Royal Infirmary, between 1933 and 1952, and 6 in the Bristol Neurosurgical centre during the past four years. In Bristol during the same period there were 21 cases of spinal tumour, 10 of which were meningioma or neurinoma. This is too small a series from which to draw deductions, but it does at any rate suggest that spinal epidural abscess is proportionally a not infrequent cause of interference with spinal cord function.

Since a presentation of the entire series would be too lengthy, the following case histories have been selected to illustrate various features of the illness.

Case 1

This case indicates the usual course of events in the acute metastatic type of infection before penicillin was available.

A youth aged 18 had malaise and fever a few hours after the extraction of an infected tooth. This was followed by an increasing low lumbar backache and pain at the back of both thighs. His temperature was 102.6° F. (39.2° C.). Acute tenderness over L 4 spinous process and severe back pain were aggravated by any movement. The abnormal neurological findings were hyperreflexia in the lower limbs, bilateral extensor plantar responses, and hyperaesthesia of the buttocks and thighs posteriorly.

The lower three lumbar laminae were removed, disclosing a localized extradural abscess containing staphylococcal pus. Pus was tracking outwards along the fourth and fifth lumbar roots. The wound was only partially closed, the central portion being left open to provide free drainage. Fever and toxaemia continued, and cerebrospinal fluid (C.S.F.) escaped from the wound. The patient died 27 days after operation.

At necropsy pus was found to have extended between the necks of the right eleventh and twelfth ribs and into the psoas sheath. A sloughing patch was found on the dura opposite the abscess and there was a generalized purulent meningitis.

Case 2

This case illustrates, in contrast, the satisfactory result obtainable by early surgical intervention and the use of antibiotics.

A healthy girl of 9 years complained of pain in the back, of fairly sudden onset. Next day the pain extended into the left thigh. Later she became delirious and was admitted to hospital with a provisional diagnosis of tuberculous meningitis. She was found to have some weakness of the left hip flexors and a depressed left knee-jerk. The left plantar response was equivocal. Lumbar puncture yielded thick staphylococcal pus from the epidural space.

Laminectomy of the second and third lumbar vertebrae was performed, and pus was found both within and external to the vertebral canal. The wound was closed in layers with indwelling tubes for instillation of penicillin into the epidural space in doses of 20,000 units twice daily for eight days. Intramuscular penicillin, 500,000 units twice daily, was continued for two weeks. The wound healed, and the patient left hospital cured, 18 days after her admission. At a re-examination eight months after operation the only residual abnormality was very slight weakness of eversion at the left ankle.

Case 3

The disastrous results of delaying operation, despite the elimination of infection by antibiotics, are indicated in this case.

A man aged 64 gave a history of septic arthritis of the knee four years prior to his recent illness; this was followed two years later by osteomyelitis of the tibia. His spinal malady began with lumbo-dorsal backache and girdle pains round his left flank and across his abdomen. Eleven days later he developed a complete flaccid paraplegia within the space of 24 hours. He also had retention of urine.

He was retained for eight days in another hospital, where a suprapubic cystotomy was done. When he was referred to the neurosurgical department three weeks after the onset of his illness he presented a complete paralysis of the lower limbs and a sensory level on the trunk at the T 10 segmental level. The *x*-ray film showed poor definition of the left pedicle of the tenth dorsal vertebra.

A laminectomy of the eighth to the eleventh thoracic vertebrae was performed, exposing red adherent granulation tissue on the surface of the dura and a few millilitres of pale yellow pus from which a penicillin-sensitive staphylococcus was cultured. The wound was closed with indwelling catheters down which penicillin (20,000 units twice daily for five days) was instilled. Systemic penicillin and sulphonamide therapy was given.

The wound healed by first intention, but though postoperative lumbar puncture demonstrated a complete absence of a spinal subarachnoid block there was no improvement in the neurological state.

Case 4

Occasionally, as in this case, the abscess is very extensive and may indeed involve the entire length of the vertebral canal. Despite this a most satisfactory result may be obtained.

A healthy child aged 2 years had a trivial fall. The next day she complained of pain in her right lower limb and of headache. She was unable to walk. A week later she developed fever and signs suggestive of meningitis. Purulent fluid was obtained on lumbar puncture. The lumbar puncture was repeated next day, and on this occasion frank pus, yielding a mixed growth of *Staph. aureus* and *Str. faecalis* was obtained.

Examination revealed weakness and some extensor rigidity of the lower limbs with extensor plantar responses; sensory testing, though inaccurate in such a young patient, seemed to show a depression of pain sensation up to the level of the iliac crests. Despite the clinical evidence of meningitis, the cisternal C.S.F. contained only 10 polymorphonuclear leucocytes per ml.

An exploration of the fenestration type was done between the laminae at L 1–2 and L 3–4 on the right side, and at L 2–3 on the left. Pus under slight pressure was released. A catheter was passed upwards extradurally through the entire length of the spinal canal, and a smaller tube down

into the sacral region. Further pus was released by saline irrigation. The wound was closed with these tubes *in situ*. Penicillin was instilled down the tubes in doses of 30,000 units, at first four-hourly and later 12-hourly.

Pyrexia subsided, and within nine days active movements of the lower limbs were noted. Two months later recovery was complete.

Case 5

This case presents an entirely different clinical pattern, and illustrates not only the prolonged course which may be followed in some instances but also the fluctuation in neurological signs and difficulty in diagnosis.

A girl aged 16, whose previous health had been good apart from a crop of boils, developed pain in the left lumbar region after playing games and doing gymnastics. The pain persisted and was aggravated by movement. Two weeks later she developed tingling and numbness in the lower limbs, followed by difficulty in walking, and increasing weakness progressing to complete paraplegia. There was impairment of sensation below the umbilicus, and retention of urine. A lumbar puncture yielded C.S.F. "under decreased tension," but unfortunately no record is available of the response to jugular compression, and the protein content was not estimated.

After about three months some spontaneous return of motor power began, and continued during the next three years. Lumbar puncture was repeated eight and a half months after the beginning of her illness and then showed no block and a protein of 30 mg. per 100 ml. of C.S.F. A diagnosis of "transverse myelitis" was made. Although she remained spastic and ataxic she was able to walk and had adequate bladder control.

Twelve years after the original onset of her illness she again suffered mid-abdominal girdle pains, and 20 days later developed complete numbness and rigidity of the lower limbs and retention of urine. This increase in neurological disability took place over a period of two days. Examination showed a complete flaccid paraplegia, sensory loss below T 11, and a complete spinal subarachnoid block. By myelography the block was localized at the level of the twelfth thoracic body.

Laminectomy T 7 to T 12 was performed, exposing dura covered with granulation tissue containing pockets of pus from which a penicillin-sensitive *Staph. aureus* was cultured. Normal dura was exposed above and below. The wound was closed with indwelling catheters, and treatment by local instillation of penicillin and streptomycin and systemic administration of the same antibiotics was undertaken.

During the past seven months there has been minimal return of motor and sensory functions in the lower limbs, but she remains virtually paraplegic, and no substantial improvement is anticipated.

In retrospect there seems little doubt that this patient suffered an acute attack of epidural inflammation with cord involvement at the beginning of her illness. This subsided spontaneously, perhaps aided by sulphonamide therapy, leaving a persisting low-grade infection which flared up again 12 years later without any known precipitating cause. Similar cases of prolonged duration with fluctuations in neurological disability have been recorded in the literature.

Case 6

This case of vertebral osteomyelitis was complicated by epidural suppuration.

A man aged 22 had an amputation through the left thigh for purulent arthritis of the knee and osteomyelitis of the femur. Shortly afterwards he experienced pain in the back of his neck, and noted some weakness of his right lower limb. The weakness improved for a time with massage, but four and a half months later the neck pain increased and he developed paralysis of his lower limb, partial loss of sensation below the lower cervical dermatomes, and incontinence of urine and faeces.

The neurological findings tended to be somewhat variable but on the whole progressive. *X*-ray films of the cervical spine showed evidence of chronic osteitis in the form of gross erosion and new bone formation in relation to the lower three cervical vertebral bodies. A marked increase in the thickness of the prevertebral soft tissues was also apparent. Lumbar puncture demonstrated a complete subarachnoid fluid block.

On exploration a chronic extradural abscess cavity with a smooth granulating wall was found. The prevertebral swelling was also explored and a small quantity of turbid fluid evacuated.

Despite drainage, the subarachnoid block remained unrelieved, and the patient died about one month after operation. Antibiotics were not available at this time. Shortly before death he developed a suprapatellar bursitis from which *Staph. albus* was cultured. It therefore seems that he continued to have a persistent pyaemia.

Case 7

The course of the illness in the more chronic type of case is illustrated by the following history.

A 45-year-old man gave a seven-months history, beginning with pain below the right scapula which radiated to the lower chest and abdomen. Three months later he sustained a heavy blow on the left lumbar region and buttock, and about a month after this experienced mid-abdominal girdle pains and an electric-shock sensation in his legs. Two weeks later, gradually increasing weakness and sensory depression in the lower limbs began. There were no sphincter or constitutional disturbances.

On examination he showed a moderate paraparesis and impairment of sensation below the eighth thoracic segment. There was no spinal tenderness. Myelography demonstrated a block at the level of the seventh thoracic vertebral body, and on exploration at this level the dura was found covered with vascular granulation tissue containing minute pockets of pus from which a haemolytic streptococcus was cultured. The wound was closed with indwelling catheters and treatment with repeated local instillation of penicillin instituted.

Gradual improvement in neurological function followed, and recovery was complete in eight months.

Case 8

This case is an example of the rare type of infection giving rise to a *true chronic granuloma*.

A man aged 36 gave a history of typhoid fever complicated by erysipelas. Since that time, for five years, he had suffered from pains in the right hypochondrium which were attributed to indigestion.

For five months he had had girdle pains at about the ninth thoracic segmental level, worse on the right side. For six weeks he had experienced pain in the back of the right knee, and tingling paraesthesiae radiating from the right side of his body down to the right knee on coughing. Two days after the onset of these pains, weakness of both lower limbs, starting on the right, began and progressed over the next four days.

Examination showed a fit-looking man with a flaccid paraplegia and sensory "level" ½ in. (1.3 cm.) below the xiphisternum. Myelography demonstrated a gradually tapering obstruction in the upper thoracic region, and at laminectomy a very vascular granuloma was exposed; this was densely adherent to the dura, and in order to relieve pressure on the cord the dura was carefully incised at the upper limit of the mass, the arachnoid being kept intact; the incision was then carried longitudinally throughout the length of the granuloma, allowing the arachnoid to bulge through. C.S.F. was seen to pass caudally beyond the obstruction.

Histologically the granuloma consisted of chronic inflammatory tissue containing aggregations of lymphocytes, and on culture yielded a Gram-negative non-motile non-lactose-fermenting bacillus which was not definitely identified.

After transitory improvement his condition deteriorated, and lumbar puncture demonstrated a subarachnoid fluid block. Re-exploration was therefore undertaken some three weeks after the first operation. The incision through the granulation tissue was found to have refilled with the same dense inflammatory mass. This was again split longitudinally and partially excised in order to free the cord, which was found to be greatly constricted at the level of the fifth thoracic lamina. There was only minimal return of motor power, and the patient died two and a half months later. Before death, *Bact. coli* and streptococci were cultured from an effusion in the knee-joint, and the blood culture yielded *Bact. coli*.

While the granuloma in this case was never definitely proved to be due to infection with an enteric type of organism, the evidence suggests that this may have been so.

Judging from the experience in this case, simple division of the constricting granuloma would appear to be insufficient to provide lasting relief of cord compression, and it seems necessary to perform at any rate a fairly generous excision of the inflammatory tissue. Even so, nutrition of the cord may perhaps be too grossly impaired by this stage for useful recovery to ensue.

Cases 9 and 10

These are examples of cases in which infection was due to direct implantation of organisms.

Case 9.—A 39-year-old man had a lumbar puncture while under investigation for headache. Some hours later he complained of pain in the back and right thigh, and two days after this he developed pyrexia with shivering which persisted despite penicillin therapy. He was acutely tender over the lower lumbar spinous processes. Epidural suppuration was suspected and exploration performed; no pus or granulation tissue was found, but a swab taken from the extradural fat showed very large numbers of polymorphonuclear leucocytes in the smear. The wound broke down and yielded thin pus, from which no organism could be cultured. Recovery was eventually complete.

Case 10.—A soldier sustained a through-and-through thoraco-abdominal wound, with the exit wound in the left buttock. The missile traversed gut, which was repaired. The patient showed a severe lesion of the cauda equina, which failed to improve. Six months after injury the cauda equina was explored and the nerve roots were freed from scar tissue. Chronic inflammatory granulation tissue was found in the epidural space. The wound was closed with tubes for instillation of penicillin. Some improvement in neurological function followed, though he remained virtually paralysed below the knees.

Aetiology and Pathology

With rare exceptions the *Staph. aureus*, usually coagulase-positive, is the causative organism. It reaches the epidural space either by the blood stream or by local extension of infection.

Haematogenous infections are derived most commonly from septic skin and subcutaneous lesions such as boils and pimples, but respiratory and urinary tract infections are among the many other possible sources of organisms.

TABLE I.—*Summary of Findings*

Source of Infection	No.	%
Cutaneous or subcutaneous suppuration	8	32
Other distant foci of suppuration	3	12
Respiratory infection	3	12
Direct implantation	4	16
? Typhoid	1	4
Not known	6	24
Total	25	100
Trauma (direct and indirect) a probable aetiological factor	9	36
Operative, radiological, or post-mortem evidence of vertebral bone or joint infection	7	28

Trauma to the spine seems to play a definite precipitating part in a number of instances, perhaps by producing a haematoma in which organisms may readily multiply.

Direct infections arise most commonly as a complication of vertebral osteomyelitis. Spread from a neighbouring suppurative lesion such as retropharyngeal abscess, probably by means of a spreading thrombophlebitis, also occurs. Direct implantation of organisms by wounds or a contaminated lumbar puncture needle is an obvious possibility. The relevant findings in the present series are summarized in Table I.

Pathological Anatomy

Although any level, and occasionally the entire length, of the vertebral canal may be involved, most cases of blood-borne infection are located in the upper and mid-thoracic region. This predilection is believed to depend on the anatomical distribution of the epidural tissue, which is of greatest thickness between the fourth and eighth thoracic vertebrae and again below the second lumbar vertebra, at which level a few cases occur. Anteriorly the theca is in contact with the posterior common ligament, and since the epidural areolar tissue is restricted to its dorsal and lateral aspects the infective lesion is similarly situated. In the present series 12 cases occurred in the thoracic and five in the lumbo-sacral region. The cervical region was involved in three cases, and the whole canal in one.

In the rare *anteriorly placed abscesses*, which occur in association with vertebral osteomyelitis, longitudinal spread is limited by adherence of the dura, but for the same reason penetration of the theca may occur, leading to a suppurative meningitis or myelitis.

In *posterior abscesses there* is much less resistance to axial spread, and pus and granulation tissue may extend widely along the spinal canal; usually, however, the extent is limited to a few vertebral segments. Cohen (1938) drew attention to the possibility of the formation of gravitational abscesses in the lumbo-sacral region from a primary focus at a higher level. In these common cases the dura forms a resistant barrier to the spread of infection, so that, although a C.S.F. pleocytosis of a few hundred cells is commonly found, a purulent meningitis is uncommon.

Not infrequently pus tracks outwards into the extra-vertebral tissue planes.

Local Pathological Process

The inflammatory reaction varies from an acute fulminating infection, with severe constitutional disturbance, to a chronic condition extending over months or even years; it probably begins as a septic thrombophlebitis initiated by a coagulase-positive organism. In most cases vascular granulation tissue containing pockets of pus of very variable size is found. In more chronic cases there is a dense adherent granuloma, often closely resembling neoplastic tissue. These chronic granulomata are much less common than the acute and subacute varieties of infection.

Despite the resistance of the dural barrier, disastrous pathological changes soon occur in the *spinal cord*; these consist of liquefaction and vacuolation in the cord substance, and microscopically of all stages of degenerative change up to death and disappearance of nerve cells and disintegration of fibre tracts. It is generally believed that these changes are caused by thrombosis or stasis in blood vessels supplying or draining the cord, a view which is supported by the rapidity with which signs of cord damage progress.

In the adult, between four and ten arteries entering the cord on each side constitute the main vascular supply to their own and neighbouring segments, by way of longitudinally disposed anastomotic vessels. The venous drainage follows a somewhat similar pattern. Stasis or thrombosis in one of these important vessels is likely to produce widespread changes, which develop early in the course of the infection and progress rapidly to a stage of irreversible damage.

Clinical Features and Diagnosis

Acute and Subacute

In most cases the illness follows a fairly constant pattern of development, and the following stages may be recognized (Rankin and Flothow, 1946; Huesner, 1948): (1) the stage of spinal ache; (2) the stage of root pains; (3) the stage of impairment of cord function, leading to sphincter disturbances, and early motor and sensory loss; and (4) the stage of complete paralysis. An antecedent history of infection, frequently of a minor cutaneous nature, is often obtainable, but this is by no means invariable.

The time relations between the several stages varies. Transition from stage 3 to 4 is usually rapid, however, and *may occupy only a few hours.* This fact is insufficiently recognized.

The onset is often fairly rapid, and accompanied by malaise and fever. The blood shows a polymorphonuclear leucocytosis, and a positive blood culture is often obtainable.

The *back pain* occurs at the level of infection; it is often agonizing, and increased by movement, especially flexion as opposed to extension (Stammers, 1938).

Tenderness on spinal percussion or pressure at the appropriate level is a most important localizing sign. There may be local swelling or redness of the skin.

Root pains, sometimes accompanied by paraesthesiae, make their appearance within a few days, or, in some cases, less than 24 hours.

Headache is common, and neck rigidity and a positive Kernig's sign are often found.

In subacute cases, and those secondary to vertebral osteomyelitis, the period of spinal ache may be more prolonged and of less severity, and the onset of root pains may be delayed for a week or two.

Careful neurological examination at this early stage will often reveal reflex changes indicative of early pyramidal tract involvement. *Lumbar manometry* shows absent or sluggish response on jugular compression, indicating a spinal subarachnoid fluid block. The C.S.F. shows an increase in protein which is of greater degree in more chronic cases, and a pleocytosis of up to perhaps 200 cells, mostly lymphocytes. This investigation is of great importance in establishing the differential diagnosis from such non-surgical conditions as transverse myelitis, and should not be omitted. It must of course be performed with care, advancing the needle a millimetre or so at a time, and aspirating frequently lest a lumbar abscess be present. With reasonable caution there is little risk of carrying infection into the theca.

The development of *stage 3,* with obvious signs of impaired cord function, occurs usually within a few days of the development of root pains. Retention of urine is often an early symptom. Pain tends to diminish with development of sensory loss.

The transition to *stage 4,* with complete motor and sensory loss below the level of the lesion, often occurs with disastrous rapidity. In seven cases in the present series, 24 hours or less elapsed between the appearance of the first neurological abnormality and the development of stage 4.

In the *chronic type of infection* the course is much more prolonged, extending over months or even years; the signs of cord dysfunction may fluctuate, sometimes undergoing spontaneous remission. The constitutional phenomena of infection are absent, and the pattern of the illness closely resembles that of extramedullary spinal tumour.

The most important factor in the diagnosis of spinal epidural abscess is awareness of its possibility. The urgency and potential gravity of these cases must be more widely recognized.

No fewer than 12 cases in the present series had a virtually complete paraplegia when presented to the surgeons. It cannot be too strongly emphasized that, once signs of interference with cord function begin to appear, the situation is one of extreme urgency and every hour of delay diminishes the chances of recovery.

Myelography may be required to establish the precise level of the lesion when the local and neurological evidence is equivocal in this respect.

Radiographs of the spine are not often helpful, since the infection in most cases is too recent to have caused visible changes in the bones.

Treatment

Once the diagnosis is established, exploration is urgently indicated. The objects of operation are (1) to release pus, and decompress the theca and its contents; and (2) to provide means for repeated local application of antibacterial substances by means of thin indwelling tubes. In the first instance a limited opening into the vertebral canal should be made by removal of ligamentum flavum and portions of adjacent laminae at one or more levels. If pus in quantity is found, this will often suffice to allow insertion of thin rubber catheters to the extremities of the abscess cavity, for repeated aspiration of pus and instillation of antibiotics.

Where the lesion consists largely of granulation tissue containing small pockets of pus, a complete laminectomy should be performed throughout the length of the infected area. If the granulation tissue is thick and dense, excision by careful sharp dissection is indicated, in order to obviate subsequent stricture of the theca by scar tissue.

In children, in whom preservation of the laminae is of importance in order to avoid the later development of a kyphosis, the laminae may be elevated in a continuous string, preserving the ligaments, so that they may be replaced at the conclusion.

The catheters are brought out through stab incisions adjacent to the main wound. In the great majority of cases primary healing can be achieved, with appropriate antibiotic therapy vigorously applied locally and systemically. An early report on the culture and sensitivity of the organism is essential. It must be emphasized that antibiotics are in no sense regarded as a substitute for early and adequate surgical intervention.

Results

The prognosis with regard to survival has undergone a dramatic change since the introduction of the sulphonamide drugs and antibiotics. Previously a fatal outcome was the rule in all acute and subacute cases not treated surgically, and also in a large number of those subjected to operation (Campbell, 1937). In Huesner's series, before 1939 there were eight acute cases with three deaths: in a group of ten similar cases after 1939 there was only one death.

The prognosis for recovery of cord function bears a close relationship to the severity of neurological deficit at the time of operation. We have been unable to establish any clear correlation between the duration of paralysis and the degree of recovery. Our impression is that once conduction in the cord becomes severely compromised it is already too late to achieve any substantial degree of recovery in most cases. This does not imply, however, that the severely paralysed case should be regarded with any less urgency, since a number of remarkable recoveries have been recorded.

The results in the present series are given in Table II.

In Table III the severity of neurological impairment at the time of operation and the subsequent degree of functional recovery in the survivors are presented.

TABLE II.—*Results*

Category	No.	Died	Survived		
			Full Recovery	Partial Recovery	No Recovery
Acute	13	4	4	3	2
Subacute ..	7	3	—	2	2
Chronic ..	5	2	1	1	1
Total ..	25	9	5	6	5

TABLE III

Degree of Neurological Deficit Before Operation	No.	Degree of Recovery		
		None	Partial	Complete
None or slight	4	—	—	4
Moderate	4	—	2	2
Complete or very severe ..	7	4	3	—

One case in which disability was mainly due to severe trauma of the cauda has been excluded.

Summary

The results in 25 cases of spinal epidural suppuration, with illustrative case histories, are presented. The importance of recognition of the urgency and potential gravity of these cases is emphasized.

The survey indicates that, with early recognition and treatment prior to the onset of gross neurological abnormalities, satisfactory recovery can be anticipated in most cases; while delay until signs of severe cord damage become apparent usually results in permanent, crippling disability.

The most important factor in early diagnosis is an awareness of the possibility of the condition, and an appreciation of the rapidity with which the pathological process advances to an irreversible state.

Acknowledgments are due to Mr. G. L. Alexander and Mr. D. G. Phillips for permission to publish the Bristol cases and for helpful advice and criticism. Cases 1 and 4–10 are from the Edinburgh series and Cases 2 and 3 from Bristol.

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LOW GAMETOCYTE THRESHOLDS OF INFECTION OF ANOPHELES WITH PLASMODIUM FALCIPARUM

A SIGNIFICANT FACTOR IN MALARIA EPIDEMIOLOGY

BY

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Malariologists have long been familiar with the inconsistencies experienced when trying to infect anopheles with malaria parasites by feeding them on patients showing falciparum gametocytes—crescents—in the blood. Those subjects with the heaviest infections have not necessarily been the most infectious—in fact, they have sometimes proved completely non-infective. Many of these discrepancies have been attributed to the great disparity in the sex ratio of the crescents, to the possibility that the gametocytes are not "ripe," and so on. Up till a few years ago, however, it was fairly generally assumed that, as the number of crescents in the blood decreased, a point was eventually reached when low density alone became a limiting factor, the subject becoming non-infective at a time when crescents could still be detected in the blood film without too much difficulty (Boyd, 1949). Those ideas seem to have been so firmly implanted that carriers with very scanty crescent infections were almost automatically rejected as a possible means of infecting anopheles in the laboratory or in the field.

Martin Young and his colleagues (1948), working with a negro population in South Carolina, showed, however, that those ideas would have to be revised considerably. They were able to infect 10 lots of *Anopheles quadrimaculatus* (nearly half of the total infective lots) at a time when falciparum gametocyte counts were less than 5 per c.mm. Of these, five cases had fewer than one gametocyte per c.mm.; and finally a few mosquitoes became infected at a time when parasites were too scanty to be detected in the ordinary microscopical examination.

Similar observations, although on a much smaller scale, were made with *Anopheles albimanus* and a negro population in Jamaica during 1950 (Muirhead-Thomson and Mercier, 1952). These observations made a particularly deep impression on us, as at that time we were unaware of the findings in South Carolina. After feeding a batch of *A. albimanus* on a 3-year-old subject who had previously been a good carrier and infector, routine examination of the thick film taken at the time of feeding failed to reveal a single crescent, and it was dismissed as negative. The mosquito batch was kept as a matter of curiosity, and one-third of them (12 out of 37) eventually developed gland infections. Later, another subject was found to be infective at a time when only a single crescent was present in over 200 thick-film fields—0.12 crescents per 1,000 leucocytes, or less than 1 per c.mm.

Present Investigation

In the Gold Coast recently this work has been continued more intensively, using laboratory-bred *Anopheles gambiae* and working in an area west of Accra where malaria is hyperendemic. In order to find out the crescent carriers and to determine the gametocyte rate of the village population—that is, the proportion showing falciparum gametocytes in first examination—thick blood films were examined rather more thoroughly than usual, no slide being dismissed as negative until at least 200, and usually more, oil-immersion fields had been examined. The gametocyte rate—or rather crescent rate—of the population examined is shown in Table I.

TABLE I.—*Incidence of P. falciparum Gametocytes in African Population. Weija, Gold Coast*, 1952

Age Group (Years)	No. Examined	No. with Crescents	% Positive (Gametocyte Rate)
0–1	52	21	40·4
2–4	62	16	25·8
5–9	148	22	14·8
10–14	78	9	11·5
15 and over	151	9	5·9

Although the gametocyte rates are rather higher than usual, the general trend is similar to that found by other workers in West Africa (Barber and Olinger, 1931; Young and Johnson, 1949; Bruce-Chwatt, 1951), the higher age groups, 15 years and over, having low gametocyte rates as well as low gametocyte densities. Heavy gametocyte infections were comparatively rare, only 1 out of 491 people examined showing over 200 crescents per c.mm. Shute and Maryon (1951), in a thin-film survey in Lagos, had the same experience, only 2 out of 800 children showing 200 or more crescents per c.mm. Higher figures have been recorded elsewhere (Barber and Olinger, 1931; Robertson, 1945; Bruce-Chwatt, 1951), but they are evidently exceptional.

The actual infectiousness of as many of these crescent carriers as possible was tested by feeding batches of 40–50 laboratory-bred *A. gambiae* on them, blood films being taken at the time of feeding. The mosquitoes were dissected four to seven days after feeding, when falciparum oocysts with their characteristic pigment (Shute and Maryon, 1952) could best be detected in the mosquito stomach. In a few of the more heavily infected batches some of the mosquitoes were kept until salivary gland infections developed.

In all, 73 batches of *A. gambiae* were fed on 32 crescent carriers of all ages from 4 months upward. Of these, 24 batches became infected from 14 carriers.

In previous work in West Africa the lowest thresholds of infection were recorded by Robertson (1945), who found four infections at thresholds below 3 crescents per 1,000 leucocytes; in one batch 1 out of 13 *A. gambiae* being infected when the crescent density was 0.7 per 1,000 leucocytes—that is, less than 5 per c.mm.

In the present investigation, of the total number of batches infected, nearly half (46%) were recorded at crescent densities below 3 per 1,000 leucocytes. On six occasions—that is, 25% of total infected batches—the crescent density at the time of feeding was below 1 per 1,000 leucocytes (Table II).

TABLE II.—*Particulars of Mosquito Infections Obtained at Falciparum Gametocyte Thresholds Below 1 Crescent per 1,000 Leucocytes*

Age and Sex of Subjects	Crescents per 1,000 Leucocytes	Mosquitoes Dissected	Positive		Mean No. Oocysts per Positive Stomach
			No.	%	
F, 2½ years	0·52	13	3	23	1·7
F, 5 ,,	0·20	21	2	9	1·5
M, 5½ ,,	0·27	20	1	5	3·0
F, 9 ,,	0·26	12	1	8	1·0
	0·10	10	1	10	1·0
M, 10 ,,	0·16	18	1	6	1·0

The two lowest figures recorded correspond to a density at or below one crescent per c.mm., the first crescent being found only after examination of 300–400 oil-immersion thick-film fields. Those slides would normally have been dismissed as negative for crescents, and it was only the knowledge that the subjects were actually infective to mosquitoes which made the search so prolonged and persistent.

From Table II it will be seen that of the total number of mosquitoes feeding on those subjects with low crescent counts the proportion infected is usually about 10% or less, and that the intensity of infection is also low—from 1–3 oocysts in each positive stomach. These figures will be seen in their right perspective if we compare them with what happens with the most infectious subjects found in this African village survey. In the four most efficient infectors found—whose crescent densities covered a wide range from 1.2 to 24.0 crescents per 1,000 leucocytes (roughly 8 to 150 per c.mm.)—it will be seen from Table III that the number of oocysts per positive stomach remains fairly low.

Of the 87 positive mosquito stomachs in this series, 76 (89%) had fewer than 10 oocysts per stomach, and only 4 (5%) had more than 20. Higher oocyst densities have been recorded elsewhere (Barber and Olinger, 1931; Robertson, 1945), but our own experience is that they are unusual, particularly after a single infective feed.

TABLE III.—*Record of Experimental Feeds on Four Most Infectious Crescent Carriers in Gold Coast Village Survey*

Age and Sex of Subjects	No. of Mosquito Batches Fed	Range of Crescent Density during Most Infective Periods (per 1,000) Leucocytes)	Total *A. gambiae* Dissected	No. with Oocysts	Intensity of Infection. Oocysts per Positive Stomach		
					Max.	Min.	Mean
M, 2 yrs.	1	6·0	18	7	26	1	9·1
M, 3 ,,	3	1·2– 4·1	50	23	28	1	5·7
M, 5 ,,	7	7·9–24·0	107	39	28	1	5·0
F, 9 ,,	5	1·7– 8·2	97	18	10	1	3·4
			272	87			

In comparing the infectiousness of these village subjects showing the lowest crescent densities (Table II) with the infectiousness of the most efficient carriers found in the survey (Table III), we can say roughly that while the best infectors will infect about 30–40% of the mosquitoes feeding on them, and produce on the average about 5 oocysts per stomach, the carriers with the lowest threshold may infect up to 10% of the mosquitoes, and produce about 1–2 oocysts per stomach. The low-threshold carriers are therefore relatively much more infective than we would imagine from their very low gametocyte densities. There is some evidence to show that such a carrier may retain a very scanty crescent infection and at the same time remain infective for long periods.

In discussing these very low gametocyte densities it must be pointed out that, as many of the figures have to be based on the finding of only one or two crescents in several hundred thick-film fields, they may possibly give a misleading idea of the true density not only in the blood film itself but also in the mosquitoes' blood meal. In fact, our findings would be altogether easier to understand if we assumed that at these low densities the distribution of crescents throughout the blood stream is very uneven.

In contrast to these low-threshold, or "cryptic," infectors, our routine tests revealed several striking examples of subjects being non-infective at a time when crescents were abundant in the blood. The most outstanding examples are shown in Table IV.

TABLE IV.—*Particulars of Non-infective Feeds at Gametocyte Densities Greater than 3 per 1,000 Leucocytes*

Age and Sex of Subjects	Crescents per 1,000 Leucocytes	No. of *A. gambiae* Found Non-infected
F, 4 months	3·3	22
F, 6 ,, ...	4·8	16
M, 2 years	7·7	13
F, 3 ,, ...	2·8	15
F, 7 ,, ...	3·9	17
F, 7 ,, ...	3·1	19

In our investigation in Jamaica (Muirhead-Thomson and Mercier, 1952), the subject with the heaviest infection remained non-infective for several weeks, while Martin Young and his colleagues (1948) report a similar failure with the two patients showing the highest gametocyte count. In this connexion it is interesting to note that in the Gold Coast village survey the highest proportion of non-infective carriers occurred in infants—0–1 year age group—only 2 out of 13 crescent carriers proving infective to mosquitoes. Whether this figure is really representative of that group or whether it is just a sampling error is obviously a point which will require further investigation.

Discussion

The first conclusion from all these findings is that the presence or apparent absence of falciparum gametocytes in routine blood-film examination may really give a very misleading idea of the infective status of the subject. Until further improvements in technique occur, actual infectiousness can be determined accurately only by test feeds with anopheles. In fact, one might go so far as to say that in trying to determine the proportion of malaria infectors in the African or native village community a more accurate picture might be obtained if test feeds were carried out on a large scale, at random, quite irrespective of the blood picture. Obviously, too, in implicating cryptic infectors, the larger the batch of mosquitoes used in the test the better. Even with batches of 40–50 anopheles one might still miss the occasional carrier who infects only 2 to 3% of the mosquitoes feeding on him. How fruitful a line of inquiry this random testing

might be is already indicated by the first tentative tests in the Gold Coast. Out of 28 adults, two young men aged about 20–25 proved infective. In view of the low gametocyte rate of this group, and the low gametocyte densities encountered under hyperendemic conditions, adults have usually been regarded as of negligible importance as a source of malaria infection. As crescent infections may occur at all ages, including the very oldest inhabitants in the community, the usual blood picture may be giving quite an erroneous impression of the infective status of this group.

The possible role of these cryptic infectors as reservoirs of malaria has also to be considered in the light of recent observations on the distribution of anopheles bites and feeds among different human age groups. With both *A. albimanus* in Jamaica (supported by observations on *A. aquasalis* and *A. bellator* in Trinidad) (Muirhead-Thomson, 1951) and *A. gambiae* in West Africa (Thomas, 1951) it has been shown that in general there is a tendency for mosquitoes to obtain the bulk of their blood meals from older children and adults rather than from infants and toddlers. From this it would appear that an adult with a cryptic infection might be a much more important reservoir of malaria than an equally infective baby, the low infectivity being counterbalanced in nature by the greater number of mosquitoes feeding on the adult.

In trying to understand the conditions leading up to malaria epidemics, or even to seasonal waves of malaria, malariologists have long been influenced by the changing gametocyte rate of the human population as found in routine blood-film examination. It is possible that the difficulties they have encountered in trying to explain the discrepancy between low gametocyte rates and densities in the human population on the one hand, and rapidly increasing infection rates among the anopheline mosquitoes on the other hand, might be due to a much higher proportion of the population actually being infective to mosquitoes for the reasons described above.

Frohne *et al.* (1950), for example, have shown in an area in South Carolina that, despite a remarkable reduction in the parasite rate of the negro population in the proportion of 318 to 1 between 1945 and 1948, infections in wild-caught anopheles still persisted. One of the explanations suggested by these workers was that a higher proportion of the human population is infective to anopheles than is indicated by the monthly parasitaemia rates. They were dealing with a strain of *P. falciparum* which had already been shown by Young and his colleagues to be capable of infecting *A. quadrimaculatus* at extremely low gametocyte densities.

Finally, it is interesting to note that these extremely low gametocyte thresholds of infection have been encountered in three different parts of the world, using three different species of anopheles, and probably as many different strains of *P. falciparum*. One feature common to all three investigations is that the human population experimented with has been negro or of negro origin. It might be worth considering how far these results could be influenced by racial characteristics.

Summary

Observations in Gold Coast villages where malaria is hyperendemic have confirmed previous findings in Jamaica, and by American workers in South Carolina, that some carriers can infect anopheles with *P. falciparum* at a time when the density of gametocytes in the blood is so low that they may be detected only with difficulty in routine blood-film examination.

In the Gold Coast experiments these cryptic carriers formed a significant proportion—roughly one-quarter of all infective carriers. This finding, together with the fact that many good crescent carriers are non-infective to mosquitoes, suggests that the blood-film examination may prove a very deceptive guide to the real malaria infectors in the African or native village community.

The implications of these findings are discussed in the light of recent work on the uneven distribution of anopheles bites and feeds among different human age groups.

The work briefly described above forms the first phase of a research scheme carried out under the control of the Colonial Office and the Colonial Medical Research Committee. It is hoped that a more detailed report will be produced at a later date.

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RHEUMATIC HEART DISEASE COMPLICATING PREGNANCY

BY

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Improvements in antenatal and intranatal care over the past 50 years have resulted in a great reduction in the maternal mortality rate. Advances in particular fields have altered the relative importance of many complications, because some which were formerly of the utmost gravity are now more amenable to treatment. The change is exemplified by an analysis of 328 maternal deaths occurring in 128,474 deliveries in the three Dublin maternity hospitals during the decade 1940–50 (O'Driscoll and Quinn, 1951), the chief causes of which were :

Eclampsia	43
Sepsis (usually complicated)	42
Rheumatic heart disease	35
Accidental haemorrhage	32
Post-partum haemorrhage	25
Ruptured uterus	21
Placenta praevia	17
Non-convulsive toxaemias	15

These figures demonstrate the importance of rheumatic heart disease as a factor in maternal mortality. No reference is made to other forms of heart disease complicating pregnancy, as few cases were seen and none was fatal.

To evaluate the problem of rheumatic heart disease in pregnancy a clinical survey was begun by us in the National Maternity Hospital on January 1, 1948, and, for the purpose of this communication, was concluded on January 1, 1952. During these years 250 pregnancies in 175 patients with rheumatic heart disease were studied. The patients were graded according to the recommenda-

tion of the New York Heart Association. The diagnosis, which was in all cases confirmed after pregnancy, was a clinical one, although electrocardiographic and *x*-ray examinations were routine. Every patient who survived was seen in 1953, so that the follow-up time varied from four years to a minimum of one year.

The average parity of these women was 4. This compares with the figure of 3.3 for all married women in Ireland. In 1,532 years of married life these women had 704 pregnancies—that is, a pregnancy every two years. Of these 704 pregnancies none was artificially terminated and only 29 failed to reach viability.

It is apparent that the number of children borne by these women was related only to their natural fertility. The series is drawn from a population which does not practise contraception, therapeutic abortion, or sterilization. The communication presents the result of uninhibited child-bearing in patients with rheumatic heart disease. Most papers on this subject are open to the criticism that indirect case selection results from these practices.

At the end of the survey 11 women had died. Five died later than one year after confinement (13, 18, 24, 36, and 36 months), and so their deaths are not thought to have been related to pregnancy. Six died during pregnancy or within one year of confinement; these deaths are considered to have been related to pregnancy. They represent a maternal mortality of 3.5%. The number of babies who left hospital alive was 229. The uncorrected foetal loss was 6.4%.

Analysis of 175 Patients

An unequivocal rheumatic history was given by 111 patients, or 63%. A strong family history was obtained in a further six cases. The incidence of the various valvular lesions was as follows:

Lesion	No. of Cases
Mitral stenosis	151
Mitral stenosis and aortic regurgitation	23
Aortic regurgitation	1

Because of the recognized difficulty in diagnosing pure mitral regurgitation (Brigden and Leatham, 1953), 10 patients with harsh mitral systolic murmurs and a personal history of rheumatic disease are grouped under the heading "mitral stenosis." In these cases the predominant defect would appear to be an incompetence of the valve. The importance of history-taking and of careful auscultation at the mitral area is illustrated by these figures.

It has often been said that the heart condition deteriorates with increasing parity. Table I confirms this, but the last column reminds us that increasing parity coincides with increasing age. This may be the relevant factor.

TABLE I

Parity	No. of Cases	Grades III and IV		Average Age
		No.	%	
1	46	15	32·6	28·5
2 to 4	83	30	36·1	33·2
5+	46	21	45·7	38·5

TABLE II

Age	No. of Cases	Grades III and IV	
		No.	%
Under 26	18	8	44·4
26 to 30	39	11	28 2
31 „ 35	48	17	35·4
Over 35	70	30	42·9

Table II shows the relative incidence of severe cases in the various age groups. With the striking exception of the youngest group, the number of severe cases increased with age. We formed the opinion that recurrences of acute rheumatism may explain the disproportionately high number in the youngest group. We believe that this constitutes a real danger to young mothers. Further reference is made to this matter.

In 17 of the 29 patients seen in acute congestive heart failure there were, apart from pregnancy, the following important relevant factors:

Auricular fibrillation	4
Auricular fibrillation and acute respiratory infection	2
Acute respiratory infection	4
Acute respiratory infection and hypochromic anaemia; Hb 32%	1
Acute pyelitis and hypochromic anaemia; Hb 23%	1
Subacute bacterial endocarditis	2
Acute rheumatism	2
Pre-eclampsia; B.P. 170/110; oedema	1

Auricular fibrillation is the most important single factor in precipitating heart failure. Its presence indicates widespread damage to the myocardium. Four additional women with auricular fibrillation were not in failure. Intercurrent infection, particularly of the respiratory tract, anaemia, hypertension, and fluid imbalance are other notable causes of cardiac decompensation during pregnancy. Active rheumatic and bacterial endocarditis caused heart failure in four of the patients in this survey.

It is of interest to note the stage at which failure occurred in these 29 patients. In two it appeared in the first trimester, in seven in the second, and in 14 between the 28th and 36th weeks, but in no instance between the 36th week and the onset of labour. Five failed during labour and one during the puerperium. This experience substantiates the opinion that the strain imposed on the heart by pregnancy steadily increases to the period between the 28th and 36th weeks, and sharply decreases in the last month. It follows that induction of labour is basically an unsound procedure in the treatment of heart disease. The comparatively small number that failed during labour indicates that, given proper management, the danger of labour has been exaggerated. The fact that only one woman failed in the puerperium lends no support to the frequent reiteration that this is a time of particular risk.

Method of Delivery

Labour was induced in three women for pre-eclampsia and in no instance for heart disease. The methods used for delivery in the 250 pregnancies were as follows:

Caesarean section	7
Forceps or breech extraction	47
Laparotomy (see maternal deaths)	1 (twins)
Died undelivered	2
Spontaneous delivery	184 (5 twins)
Evacuation of incomplete abortion	4
Complete abortion	5

The incidence of caesarean section was 3%, whilst in the whole hospital service it was 1.5%. This discrepancy arose as the result of cases operated on more than once before coming under our care.

Only one caesarean section was performed for heart disease. It was in the early stages of the survey. The patient was subsequently delivered vaginally of her second baby. This illustrates the attitude towards abdominal delivery prompted by the intervening cases. The operation was performed in error resulting from inexperience of this condition. We now believe that rheumatic heart disease is never an indication for section.

Caesarean section was performed once for central placenta praevia, once for severe pre-eclampsia at 30 weeks' gestation and once for absolute disproportion. From fear of rupture of the uterus three operations were carried out on women who had undergone section at least twice previously for heart disease. The cardiac condition did not influence the decision in any of the foregoing six cases.

Six women who had undergone section previously for heart disease were delivered by the natural passages. The assisted vaginal delivery rate of 20% was twice the rate for all the hospital deliveries. The timely but not routine forceps or breech extraction is favoured. Local analgesia, supplemented when necessary by intravenous thiopentone, was used in all operative deliveries.

Maternal Deaths

Six women died during pregnancy or within one year after. A brief description of each follows :

Case 1.—Primigravida aged 25. Emergency admission at 31 weeks' gestation with subacute bacterial endocarditis complicated by embolic hemiplegia. Labour began spontaneously one week later and was terminated by breech extraction. The endocarditis did not respond to treatment, and the patient died 10 weeks after delivery from congestive heart failure. The baby survived.

Case 2.—Primigravida aged 28. Emergency admission at 30 weeks' gestation, moribund from congestive heart failure (grade IV). She was not in labour and died undelivered 12 hours after admission. This patient had mitral stenosis and aortic incompetence. She had been having frequent attacks of haemoptysis for three months before admission and had been partially incapacitated by her heart for several years.

Case 3.—Primigravida aged 24. Emergency admission at 16 weeks' gestation, moribund from congestive heart failure (grade IV). She was not in labour, and died one hour after admission. She had mitral stenosis and aortic regurgitation. No antecedent history was available.

Case 4.—Primigravida aged 23. Emergency admission at 30 weeks' gestation with cardiac decompensation (grade IV). There was considerable enlargement of the heart, tachycardia, and extrasystoles. She had aortic regurgitation and mitral stenosis. Her condition improved considerably in hospital, but frequent bouts of tachycardia were accompanied by relapse into failure. A diagnosis of active rheumatic carditis was made; she had an easy labour at term, ending in low forceps delivery. The baby survived, but the mother died six weeks later from congestive heart failure.

Case 5.—Gravida 2 aged 27. Emergency admission at 32 weeks' gestation with cardiac decompensation of moderate degree (grade III) due to acute bronchitis. She responded well to treatment, ceasing to be a cause of anxiety until three weeks before term. She then developed pneumococcal pneumonia involving the right upper lobe. This caused acute cardiac distress and a fulminating bacterial toxaemia which precipitated the onset of labour 17 hours later. Despite an easy rapid labour lasting six hours, she died five hours after spontaneous delivery in congestive failure; the baby was stillborn.

Case 6.—Gravida 10 aged 39. Emergency admission at 30 weeks with unexplained pyrexia and a twin pregnancy. Her last delivery had been by classical caesarean section for placenta praevia outside our service. On admission her general condition was poor, temperature 100° F. (37.8° C.), pulse 128, haemoglobin 23%, blood pressure 160/90, albumin, a trace; she had mitral stenosis, with considerable enlargement of the heart, and was in congestive heart failure. Subacute bacterial endocarditis was diagnosed, and she was treated with fair response. Her general condition deteriorated again at 34 weeks, and on further investigation it was clear that her symptoms were due to quiet rupture of the uterus. At laparotomy two macerated foetuses and their placentae were in the abdominal cavity, which was heavily infected. A loop of small gut was torn where it adhered to the uterus. Subtotal hysterectomy and bowel resection were performed. The patient died 24 hours later.

All six who died were unbooked patients; not one had received antenatal care at the hospital before admission to the wards in heart failure. There was a 20% fatality rate in unbooked patients. No booked patient died. This emphasizes the importance of routine examination of the heart of every midwifery patient. It also emphasizes the importance of efficient antenatal care. It has been our experience with emergency admissions that frequently neither the patient nor her doctor knew that heart disease existed until symptoms of heart failure appeared. The explanation is that many practitioners do not examine the heart of a pregnant woman because they are unaware of the frequency and gravity of heart disease. This fact demands the attention of all engaged in teaching obstetrics.

A striking feature of the fatal cases was the preponderance of the young and the primigravidae. The only exception was Case 6, who would probably have survived if her uterus had not ruptured. Was it because these women were young or because they were primigravidae that they died; or were these matters merely of coincidence ? Three of these fatal cases had aortic incompetence.

Case 1 died from subacute bacterial endocarditis 10 weeks after an easy delivery. It may be assumed that neither age nor parity was of importance here. Case 5 died in congestive failure precipitated by lobar pneumonia and aggravated by the untimely onset of labour, albeit rapid and easy. This death was not influenced by age or parity. Case 4, a primigravida aged 23, died six weeks after a normal delivery. She was under our care long enough for us to be satisfied that the deterioration of her heart was due to active rheumatic carditis. This was related to her age. Case 3 died from congestive failure at 16 weeks' gestation. She was 24 years old, and we suggest that her youth exposed her to a recrudescence of acute rheumatism. Her parity was hardly an important factor. Case 2 died similarly, in congestive failure at 30 weeks' gestation. That she was a primigravida was not likely to have been of importance, because she was not in labour. A rheumatic recurrence is offered to explain this fatality in a woman of 28 years.

It is our opinion that age and parity were matters of simple coincidence in Cases 1, 5, and 6, and that age rather than parity was an important factor in Cases 2, 3, and 4. The young mother who is by coincidence usually a primigravida is prone to reactivation of her disease, and we agree with others that this is of the greatest importance in determining a fatal issue (McKeown, 1948, 1950; Kennedy, 1950; Castleden *et al.*, 1951).

Paradoxically, most of the deaths occurred in the groups which contained the smallest number of severe cases—that is, in the younger women and women of low parity. Although most of the patients in failure were older and of high parity, only one of these died, and she as the result of a ruptured uterus. None of the women with fibrillation died. The inference is that the heart damaged by rheumatic disease is not likely to result in death if proper care be given, unless the mother's youth exposes her to the risk of reactivation of the disease.

The five women who died more than a year after delivery were all amongst the older age groups (33, 35, 37, 37, and 48 years), and all died from heart failure. They had reached the end phase of their disease. The fact that they survived their latest pregnancy by more than a year suggests that pregnancy did not contribute to these deaths.

Contraception, Therapeutic Abortion, and Sterilization

Contraception, therapeutic abortion, and sterilization are not practised in this city. There were 229 healthy surviving children born to these 175 women in the four-year period. It is of interest to consider the effect that the absence of these practices had on the maternal survival rate.

Women with heart disease are commonly advised to have only two children, and to ensure this the patient is often sterilized after the second delivery. Had this procedure been adopted in our series many operations would have been done, as a result of which one woman would have been saved from death due to rupture of the scar of a classical section carried out for placenta praevia.

All six women who died were seen too late in pregnancy or too advanced in heart failure for therapeutic abortion to be performed. Since no woman who received antenatal care at the hospital was lost, one might be justified in assuming that proper antenatal care would have been more likely to save them than therapeutic abortion.

It is unlikely that the practice of contraception would have affected the mortality from heart disease, since four

women died on their first pregnancy, and the only one who died later than the second pregnancy did not die from heart disease.

Had sterilization, abortion, and contraception been considered in the management of these cases they would have been applied to those who survived and not to those who died.

The dangers of these procedures have never been systematically presented. The indications, ages, parity, and maternal mortality figures in a series of cases treated by these methods would render an assessment of their advantages, or otherwise, possible. Until such figures appear it seems that good antenatal care can be expected to serve a mother better than either therapeutic abortion or sterilization.

Outcome of 250 Pregnancies

Of the 250 pregnancies observed, six were twin pregnancies. The outcome may be summarized as follows :

Surviving infants	229
Stillbirths	10
Neonatal deaths	6
Abortions and miscarriages	9
Died undelivered	2

Estimating the percentage of stillbirths and neonatal deaths on the number of infants delivered (245) who weighed more than 2 lb. 12 oz. (1.25 kg.), we obtain the figures of 4% and 2.4% respectively. The corresponding figures for all deliveries in the hospital over the same period were 3.8% and 2.4%.

Two of the stillbirths were examples of hydrops foetalis ; rupture of a classical section scar in a case of twin pregnancy caused the death of two infants ; two infants died as the result of extensive placental infarcts due to pre-eclampsia (one of these mothers suffered from diabetes) ; a central placenta praevia caused another stillbirth ; and one was a macerated twin, its fellow surviving. In none of these eight cases did the maternal heart condition affect the foetal loss. In the other two cases of stillbirth the mothers were suffering from cardiac decompensation, but it is likely that the stillbirths would have otherwise resulted : one mother suffered from primary uterine inertia, and the foetal heart ceased after labour had lasted 80 hours ; the other was suffering from an overwhelming toxaemia due to acute lobar pneumonia.

Not one of the six neonatal deaths was related to maternal heart disease. Two resulted from congenital malformations, one was caused by pneumococcal meningitis, and one by laceration of the tentorium cerebelli. One baby was found to have atelectasis following prolapse of the cord, and another suffering from laryngismus died suddenly when 6 days old. Each case was examined at necropsy.

The nine abortions or miscarriages give the surprisingly low incidence of 3.6%. The incidence of abortions and miscarriages in the hospital over the same period was 7.5%. As many women do not attend in early pregnancy and abort outside hospital, these figures may not be reliable. But the figure for the heart cases seems to be confirmed by the fact that these women had borne, in all, 704 pregnancies, including those under consideration, and only 29 (4%) had terminated before the period of viability. It can be confidently stated that none of the nine abortions or miscarriages were caused by rheumatic heart disease.

In the case of the two women who died before delivery the foetal loss can clearly be attributed to the heart condition.

Since rheumatic carditis did not affect the survival of more than four conceptions in 256 it seems fair to assume that the prospects of a healthy child in a woman who suffers from this disease is virtually the same as in one who does not. In assessing these figures it must be remembered that therapeutic abortion was not performed, so that 89.5% of all conceptions seen at the hospital resulted in surviving children.

Conclusion

As already stated, the cases recorded in this paper were totally unselected ; contraception, termination, and sterilization were never practised. Furthermore, the patients were mainly drawn from the under-privileged groups, with poor home conditions and no home help, who are fertile to a degree which workers in other countries rarely see.

Diagnosis is the first and clearly the most important aspect of the problem of rheumatic heart disease in pregnancy. That it is simple is illustrated by the preponderance of mitral stenosis and the frequency of a rheumatic history. The functional systolic murmur so common in pregnancy may lead to the suspicion of disease more often than it exists, but failure to recognize existing disease is a more serious error. In the present series all of the fatalities occurred in cases which were not diagnosed until failure was established.

Rest is the natural sequel to diagnosis. Cases without significant limitation of cardiac reserve are allowed to go home. They are advised specific rest hours, which are systematically increased until they are admitted to hospital two weeks before term. Patients with limitation of cardiac reserve are admitted to hospital without delay and are not discharged until after delivery. The importance attached to rest is signified by the total of 5,250 days which the women in the present series spent in the antenatal wards of the hospital—that is, an average of 21 days before each delivery.

Digitalization, diuresis, venesection, etc., are adopted as in the standard management of heart disease. Valvotomy is now an additional weapon.

Heart disease is not regarded as an indication for induction of premature labour or for caesarean section. Forceps extraction is often employed to abbreviate the second stage of labour. Post-partum haemorrhage is never encouraged or permitted to continue, venesection being a much safer method of reducing the circulatory volume when necessary.

Summary

The case histories of 175 women in 250 pregnancies over a period of four years are analysed.

Rheumatic heart disease is a common complication in pregnancy (1.7%).

The diagnosis is a simple clinical one.

Early diagnosis is imperative if fatalities are to be avoided.

There was no maternal death in 220 booked cases.

It is considered that there is no place for therapeutic abortion or sterilization.

This survey was begun during the Mastership of Dr. A. W. Spain. We are grateful to him for his interest and stimulating advice.

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A revised edition of *Social Work* is now available in the "Careers for Men and Women" series issued by the Ministry of Labour and National Service (H.M.S.O., price 1s. 6d.). Information is given on the scope of each career, the pre-entry qualifications needed, the amount, cost, and type of training required, and the professional opportunities available after qualification. Among the careers described in the booklet are almoner, psychiatric social worker, mental health officer, moral welfare worker, home teacher of the blind, and family case worker. This is a useful booklet for anyone likely to be asked for advice in the choice of a career closely related to medicine.

SUXAMETHONIUM (SUCCINYLCHOLINE) CHLORIDE AND MUSCLE PAINS

BY

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In normal human subjects both decamethonium and suxamethonium salts act by depolarization, the onset of paralysis being preceded by a momentary period of stimulation which is often visible as muscle fasciculations throughout the body. Conscious volunteers have often noted the characteristic tight feeling in the jaw and calf muscles that may persist for 12 to 24 hours after an injection of decamethonium (Organe *et al.*, 1949; Churchill-Davidson and Richardson, 1952). An investigation has been carried out to determine whether similar muscle pains follow the injection of suxamethonium.

Method

For this investigation the patients were divided into two groups. Group I comprised those out-patients undergoing minor operative procedures necessitating a general anaesthetic and muscular relaxation—that is, bronchoscopic and laryngeal investigations. Group II was identical with Group I except that the patients were confined to hospital for at least 48 hours after the operation.

On the second post-operative day each patient was asked to complete Form 1.

FORM 1

1. Were you able to return to work the next day? If the answer is "no," would you please give the reason.
2. Did you sleep well the night after the examination?
3. Did you have any pain or weakness in your muscles the following day? If the answer is "yes," would you please give as many details as possible.
4. Did you have any headache following the examination? If so, for how long?

Questions 1, 2, and 4 were included merely for padding. If the answer to question 3 was "Yes" the patients were asked to complete Form 2 on the fourth post-operative day.

FORM 2

(*a*) When did the first pain occur? (E.g., that evening, next morning, afternoon, etc.)

(*b*) Where did you first notice it? (E.g., all over the body, in neck, or in legs, etc.)

(*c*) Is it similar to any other pain you have experienced? (E.g., cramp, stiffness, pins and needles, etc.)

(*d*) How long did it last? (E.g., one hour, six hours, one day, three days, etc.)

(*e*) Did anything make it worse or better? (E.g., improved on exercise or improved on resting.)

Premedication.—The patients in both groups were given papaveretum hydrochloride, 10 mg., and hyoscine hydrobromide, 0.425 mg., except those over 60 years of age, who were given 10 mg. of papaveretum hydrochloride and 0.6 mg. of atropine sulphate.

Anaesthesia was induced with 0.3–0.5 g. thiopentone sodium (mean dose, 0.46 g. in group I and 0.42 g. in group II), followed by 30–150 mg. suxamethonium (mean dose, 88 mg. in group I and 96 mg. in group II).

Age Incidence.—Each group was selected at random. The average age in group I was 58 years and in group II 64 years.

Results in Group I (Out-patients)

Of 32 cases examined, 21 (66%) developed muscle pains on the day after the operation, and in two-thirds of these 21 cases the pains appeared to be of a severe and incapacitating nature (Table I).

TABLE I.—*Details of Muscle Pains Present in* 21 (66.7%) *Out of* 32 *Cases Examined*

Site:	Generalized, 13 (61.9%); legs and arms, 6 (28.6%); subcostal region only, 2 (9.5%).
Description:	"Stiffness," 14 (66.7%); "weakness," 4 (19%); "rheumatic," 3 (14.3%).
Duration:	4 days, 3 (14.3%); 3 days, 7 (33.3%); 2 days, 8 (38.1%); 1 day, 3 (14.3%).
Severity:	Severe, 14 (66.7%); moderate, 2 (9.5%); mild, 5 (23.8%).
Relief:	By exercise, 14 (66.7%); by rest, 7 (33.3%).

The severity of these muscle pains following suxamethonium is best emphasized by brief reference to three case histories.

Case A.—A conscious volunteer subject was given 10 mg. of suxamethonium intravenously. A brief period of skeletal muscle paralysis ensued (approximately 3 minutes 20 seconds). Recovery was rapid and complete. No further trouble was experienced until on rising the following morning, when he felt a generalized stiffness with a painful sensation in the subcostal and retrosternal region. The stiffness gradually receded during the day, but the subcostal pain persisted for a further two days.

Case B.—A woman aged 26 attended hospital as an out-patient for bronchoscopy following a persistent *x*-ray shadow at the base of the left lung. She was anaesthetized with 0.4 g. of thiopentone sodium and 100 mg. of suxamethonium. Three hours later (5 p.m.) she left hospital feeling well, and during the rest of the evening was able to carry out her normal household duties. On awakening next morning, however, she was hardly able to move her arms or legs, and had to be assisted into the upright position. There was only slight improvement throughout the day. Next day she stated that her legs still felt too weak to stand, and she was brought to hospital in an ambulance. On examination the range of passive movement in the limbs was almost complete, apparently being only slightly limited by pain. Reflex activity and sensation were normal. There was marked reduction in active movement, particularly in the lower limbs, with some tenderness on pressure of the muscles.

Case C.—A man aged 67, with carcinoma of the bronchus, was anaesthetized with 0.4 g. of thiopentone and 90 mg. of suxamethonium for bronchoscopy. Next day he was well and left hospital in the afternoon. As he was climbing the stairs of his home his legs felt painful and weak. This persisted to such a degree that he was readmitted to hospital the same evening, although no cause for the weakness could be found.

Comment.—Cases B and C clearly showed a certain accompanying psychological element, but in the light of the evidence presented in Table I they cannot be dismissed as hysterical. Some of the patients described their condition with such phrases as "unable to move next day," "lost strength in all muscles," and "ached all over," to mention but a few.

Results in Group II (In-patients)

Of 36 patients examined, only 5 (13.9%) complained of muscle pains, and full details of these pains are shown in Table II. It is interesting to note that of the five patients who complained of muscle pains three had been permitted to leave their bed either on the same night or on the follow-

TABLE II.—*Details of Muscle Pains Present in* 5 (13.9%) *of* 36 *Cases Examined*

Site:	Generalized, 1 (20%); legs and arms, 2 (40%); subcostal, 2 (40%).
Description:	Stiffness 5 (100%).
Duration:	3 days, 1 (20%); 2 days, 3 (60%); 1 day or less, 1 (20%).
Severity:	Severe, 1 (20%); moderate, 0; mild, 4 (80%).

ing day. If, therefore, only those patients who remained at rest are included, the incidence of muscle pains in this group is 5.6%—that is, 2 patients out of 36 examined.

Trial with Gallamine

In order to determine whether the abolition of visible muscle fasciculations prevented the muscle pains following suxamethonium a further series was attempted identical with group I (out-patients) except that the injection of suxamethonium was preceded by 40 mg. of gallamine triethiodide. This abolished visible twitching in every case. Of 15 cases examined, 6 (40%) complained of muscle pains. The significance of results based on such a small series is difficult to analyse, but the general impression was that following gallamine the incidence and severity of the muscle pains were diminished, though with this dosage they were not abolished. Further support is given to this suggestion by the finding in 12 in-patient cases (that is, confined to bed for 48 hours after operation), that if a dose of gallamine triethiodide (80 mg.) was given before the administration of suxamethonium there was no case of post-operative muscle stiffness.

Discussion

Suxamethonium has been widely used as a short-acting muscle relaxant in both clinical surgery and electric convulsion therapy. If it is given, however, to patients who are not confined to bed after treatment it may be followed by a degree of incapacity out of all proportion to the severity of the procedure. Severe stiffness can develop on the first day after operation, which has been likened to the muscle stiffness that often follows some violent physical exercise. If, on the other hand, the use of suxamethonium is confined to patients resting in bed the incidence of muscle pains is low.

It has been shown in man that decamethonium iodide causes muscle activity of apparent motor unit origin (Churchill-Davidson and Richardson, 1952) as opposed to single muscle-fibre potentials which might be anticipated from the use of a depolarizing drug. It has been suggested (Paton, 1952) that this fascicular twitching is due to centripetal antidromic impulses in the motor nerve axon bringing about a synchronous discharge of the whole motor unit (Masland and Wigton, 1940). The finding that gallamine triethiodide prevents the muscle fasciculations of suxamethonium but only reduces the incidence of "after-pains" suggests that these pains may not be due to the vigorous twitching of the muscles but to some curious association of depolarization by succinylcholine and normal muscular activity.

Suxamethonium, therefore, has two serious disadvantages. First, in company with all depolarizing drugs it has no satisfactory antidote, and the occasional case of prolonged action still occurs (Bourne, 1953; Evans *et al.*, 1952). Secondly, it is unsuitable for use as a muscle relaxant for out-patient procedures, because it may be followed by severe muscle stiffness.

Decamethonium enjoyed only a brief span of popularity in clinical surgery. It would seem that the longevity of suxamethonium must depend upon the time it takes to find a new muscle relaxant of brief effect acting by competitive inhibition (like D-tubocurarine chloride) but destroyed by plasma cholinesterase. In the event of a prolonged action neostigmine could then be given with confidence.

Summary

When suxamethonium is used as a short-acting muscle relaxant for out-patient procedures it is followed next day in a large proportion of cases by muscle pains and stiffness, the severity of which is out of proportion to that of the minor operation. These pains commonly persist for two to three days. The incidence in patients confined to bed is low.

The abolition of the fascicular twitching—a notable feature after the injection of suxamethonium—reduced the incidence and severity of the muscle pains.

The value of suxamethonium as a short-acting muscle relaxant is briefly discussed.

I am most indebted to Drs. Regina Mackay and David Chandler for their help in following up these cases, and to all the members of the department of anaesthetics who co-operated so generously. Miss Jean Davenport gave invaluable secretarial assistance.

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ACUTE TOXIC HYPOGLYCAEMIA IN THE VOMITING SICKNESS OF JAMAICA

BY

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The illness at present known as the vomiting sickness of Jamaica has a distinct clinical picture, which has been reviewed by Hill (1952). It occurs sporadically or in small, usually family, outbreaks during the colder winter months, when food is relatively scarce amongst the Jamaican peasant population. The onset is dramatically sudden, often with severe vomiting, followed by rapid prostration with a low blood pressure and tachycardia; the temperature is not elevated and diarrhoea does not occur. This may be followed by a latent period of apparent improvement lasting a few hours or may pass direct into the terminal phase of drowsiness, twitching, convulsions, and coma—sometimes associated with effortless vomiting. There is a high mortality, death occurring on an average after 12 hours. Cases that recover do so completely.

A fulminating clinical variant is also recognized in which no vomiting occurs, the illness presenting with spectacular abruptness, with sudden collapse, drowsiness, convulsions, stupor, twitching of the limbs, coma, and death. The whole episode may last only a few hours.

The syndrome usually occurs against a background of poverty and subnutrition, and those affected are often, but not always, underweight and frequently show signs of slight deficiency of the vitamin-B complex and protein—such as angular stomatitis, glossitis, mosaic skin, and hypochromotrichia. Families are often involved, the main incidence being in children of 3 to 10 years.

As has been stressed by Cicely Williams (1953) and Chambers (1953), a diagnosis of vomiting sickness is often loosely used in Jamaica to cover various undiagnosed illnesses in which vomiting or sudden death has occurred. Nevertheless, after taking this into account, there remains a definite group of typical cases showing a characteristic clinical picture.

Aetiology

The precise aetiology of the vomiting sickness of Jamaica is still very much in doubt and cannot be discussed here fully. The various hypotheses have been considered by Hill (1952). Meningitis, encephalitis, cerebral malaria, and other acute cerebral inflammatory diseases can be excluded both clinically and by post-mortem evidence. The present consensus of opinion is that the syndrome is due to the effect of an unknown poison, or possibly one of several poisons, upon subjects who are usually rather poorly nourished, especially children. Metallic poisons, botulism, "barracuda poisoning" (from fresh but diseased fish), and the staphylococcal toxin have all been suggested on occasion with no real evidence; while ill-prepared bitter cassava or unripe yams—both of which contain cyanogenic glucosides—are sometimes alleged to be responsible, although again there seems to be little proof.

The ackee (*Blighia sapida*), which is widely grown and eaten throughout Jamaica, has been shown to contain a toxic saponin when immature (Evans and Arnold, 1938). Scott (1916), in his investigation of this subject, concluded that all cases were due to the eating of unripe ackees, and he was of the opinion that the disease should be called "ackee poisoning." However, as Cicely Williams (1953, personal communication) notes: "In spite of the evidence produced by former workers that the ackee was responsible, it is difficult to reconcile this with the fact that most Jamaicans are eating ackees regularly. They eat them in large quantities. Some people eat them raw or eat the fruit before the 'pod' is opened. They even drink the 'pot-water' after boiling the ackees, without disaster in the majority of cases." Nevertheless, most observers feel that the unripe ackee should still be suspect. Finally, it may be noted that herbal infusions of "bush tea," which are universally used as beverages and medicinally, are made from a very wide variety of plants which may conceivably be sometimes misused, with toxic results.

An unusual feature of the syndrome of vomiting sickness is that it has not been described elsewhere in the world, even in the other Caribbean territories.

Actual field investigations of cases of vomiting sickness are usually inconclusive, owing to the difficulty of obtaining accurate medical histories and because of the large number of potentially poisonous plants—including the ackee tree—to be found in the bush around the average Jamaican peasant's home. The dietetic history of children under these circumstances is even more difficult to assess, as, although the family's diet may be known, during the "hungry months" ill-fed children may scavenge in the bush and experiment with wild berries, fruits, and plants.

During the first three months of 1953 a number of cases of vomiting sickness were admitted to hospital here showing a vivid and pathogenic clinical picture associated with severe hypoglycaemia. Clinical details of these cases are in the process of publication (Stuart, Jelliffe, and Hill), as is a discussion of the pathology (Hill and Bras). The following is the description of a case seen more recently.

Case Report

A 6-year-old Jamaican boy of African extraction had been quite well until 4 p.m. on the day before admission, when he had vomited once, bringing up a small quantity of undigested food. There was no abdominal pain or diarrhoea. Following this the child had appeared to be quite well and went to bed normally at 9 p.m. He passed urine during the night at 1 a.m. and 6 a.m., and on each occasion he was seen by his father, who thought he appeared to be quite well. At 7 a.m. the father called the child for his morning "bush tea," but could not wake him. The father thought the boy was in a deep sleep, but on trying to rouse him 15 minutes later the child was found to be unconscious, with his legs in rigid extension, arms tightly flexed on his chest, hands clenched, and jaw locked. This stiffness seemed to wax and wane, lasting about 10 minutes with longer intervals between.

The rest of the family, consisting of the father and a 3-year-old sister, were in no way affected, although they had all eaten the same meals together. The patient had eaten no ackees or other possibly toxic substances during the preceding 36 hours, so far as the father was aware, although there were plenty of ackee trees and other bushes around the house.

The patient arrived in the ward at 2 p.m., when he was found to be deeply comatose with stertorous respiration. He was afebrile, with a pulse of 120 and a blood pressure of 110/60. There were no signs of meningeal irritation. The eyes tended to rove about, with a transient squint. The fundi and pupils were normal. The limbs were flaccid at the first examination and all tendon reflexes were diminished. Painful stimuli produced no response, while the abdominal and plantar reflexes were absent. The child was well hydrated and moderately nourished, with only minor stigmata of malnutrition, in particular slight angular stomatitis and cheilosis. The liver was just palpable.

During the first three-quarters of an hour after admission there were repeated attacks of stiffening of the limbs, each lasting about one to two minutes, accompanied by a rigor-like shaking. During these bouts the limbs became hypertonic with greatly increased reflexes.

In view of experience gained with previous cases, a diagnosis of acute toxic hypoglycaemia due to vomiting sickness was made.

Investigations.—Investigations carried out immediately on admission showed: (1) Blood count: haemoglobin, 11.6 g. per 100 ml.; red cells, 3,500,000 per c.mm.; white cells, 17,000 per c.mm. (metamyelocytes 0.5%, neutrophils 85%, lymphocytes 14.5%); E.S.R., 6 mm. per hour; haematocrit, 32%; M.C.V., 91.4 μ^3; M.C.H.C., 36.3%; M.C.H., 33.1 $\mu\mu$g. (2) Liver-function tests: bilirubin (total), 0.6 mg. per 100 ml.; cephalin-cholesterol flocculation test, negative; gamma-globulin (Kunkel), 5.8 units; thymol flocculation, negative; thymol turbidity, 1.2 units; serum proteins, total 7.4 g.% (albumin 4.9 g., globulin 2.5 g.); cholinesterase

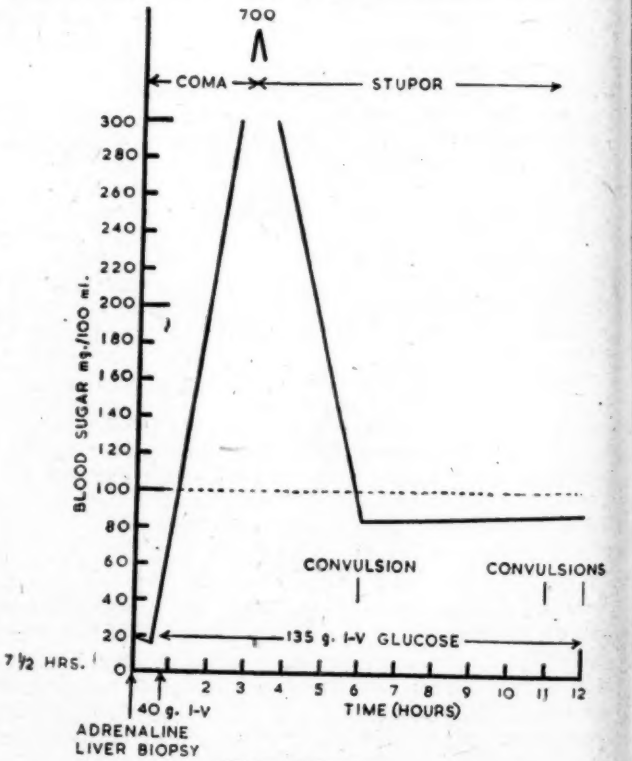

Chart of the case.

(Michel), 0.7 unit. (3) Blood urea, 45 mg. per 100 ml. (4) Serum calcium, 11 mg. per 100 ml. (5) Carbon dioxide combining power, 40 volumes per 100 ml. (6) E.C.G., normal. (7) Blood sugar, 19 mg. per 100 ml. (8) Liver biopsy (immediate): almost complete absence of liver glycogen (0.7%).

Progress in hospital is summarized in the accompanying graph. Adrenaline, 5 minims (0.3 ml.), was given subcutaneously on admission and the blood sugar was estimated after 15 minutes. This showed no real change (18 mg. per 100 ml.). Treatment was then begun with an injection of 40 g. of glucose intravenously, in a 50% solution, followed by a continuous intravenous drip of 9.5% glucose solution. By 4.25 p.m. the blood sugar had risen to 700 mg. per 100 ml. and was associated with a marked glycosuria. No dramatic clinical effect was produced, although the coma appeared to be definitely lighter during the afternoon and evening. The blood sugar had fallen to 84 mg. per 100 ml. by 8.30 p.m., and thereafter remained between 80 and 100 mg. The child continued in a stuporose condition, and during the night he had two generalized tonic-clonic convulsions. Next day a further fit occurred at 5 a.m., following which the child died, the respiration stopping while the heart continued to beat for 15 minutes afterwards.

Post-mortem examination was mainly negative save for lymphoid hyperplasia in the mesentery and ileum, together with fatty change in the liver.

Discussion

The very low blood sugar and almost absent liver glycogen found in this case have also been noted in other examples of vomiting sickness investigated during the acute phase of the illness. Full clinical and pathological details are to be published elsewhere, but results from five cases, including the present one, are summarized in the Table. The rapid

Details of Five Children Admitted with Acute Toxic Hypoglycaemia in the Vomiting Sickness of Jamaica

Case No.	Age in Years	Sex	Mental Condition on Admission	Blood Sugar (on Admission) (mg. per 100 ml.)	Known Length of Coma (Hours) before Treatment	Response to Large Doses I.V. Glucose
1	6	M	Drowsy	6	—	Rapid recovery
2	5	F	Comatose	3	2	Slow recovery (32 hours)
3	8	F	Drowsy—comatose (fluctuant)	5	4	Rapid recovery
4	4	F	Comatose	15	11	Slight improvement. Died
5*	6	M	"	19	7½	" "

* Present case.

onset, with or without vomiting, of various grades of cerebral depression—varying from drowsiness to stupor to coma—have been observed. Some early mild cases have responded dramatically and immediately to large doses of intravenous glucose, while others have recovered after some hours of treatment.

The present case can be regarded as a fulminant example of so-called vomiting sickness—coma coming on in only one hour, if the father's story is to be believed, while vomiting was virtually absent. Clinical response to a large dose of intravenous glucose was very slight, possibly because of the relatively long period—seven and a half hours—elapsing between the onset of coma and the beginning of treatment. The prognosis in these cases seems directly related to this interval, possibly because irreversible changes can be produced if hypoglycaemia is prolonged.

The toxin responsible for this dramatic clinical syndrome is unknown, but is very probably an accidentally ingested poison, possibly from some wild plant used in one of the "bush teas." The biochemical mechanism producing the hypoglycaemia is also as yet undetermined, but it seems likely that some form of enzyme blockage may be produced, possibly in the enzyme systems responsible for hepatic gluconeogenesis. Whatever this may be, it is temporary and potentially reversible, as if recovery occurs, either spontaneously or following intravenous glucose, it is complete.

While hypoglycaemia is the most striking biochemical finding, there may be other upsets of blood chemistry as yet undiscovered. However, the presence of very low blood sugars in these cases does offer a possible immediate line of therapy, and it seems logical that cases of vomiting sickness should now be treated as medical emergencies with intravenous injections of concentrated glucose solution as soon as possible after the onset of symptoms.

Our thanks are due to Dr. G. Bras for carrying out the necropsy, and to Dr. S. J. Patrick for analysing the liver for glycogen.

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CONGENITAL ABSENCE OF BOTH KIDNEYS

A REPORT OF FOUR CASES

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Agenesis of both kidneys is a rare condition, only 171 cases having been reported since 1663. The four cases occurring at the West Middlesex Hospital described by us bring the total to 175.

The largest number reported was 20 by Potter (1946a, 1946b). These she found in a series of 5,000 necropsies on foetuses and newborn infants, and she estimated the incidence to be 0.3 per 1,000 births. At the West Middlesex Hospital the incidence was four cases amongst 9,940 deliveries (that is, 0.4 per 1,000 births).

The absence of both kidneys is usually accompanied by other gross or multiple deformities (Hinman, 1940). The sex incidence is predominantly male. Bilateral agenesis is compatible with intrauterine life, and does not appear to affect the quantity of liquor amnii. Survival after birth is short; the average duration of life in Potter's cases was 1½ hours. One case is reported to have lived for as long as 21 days, and another for 11 days.

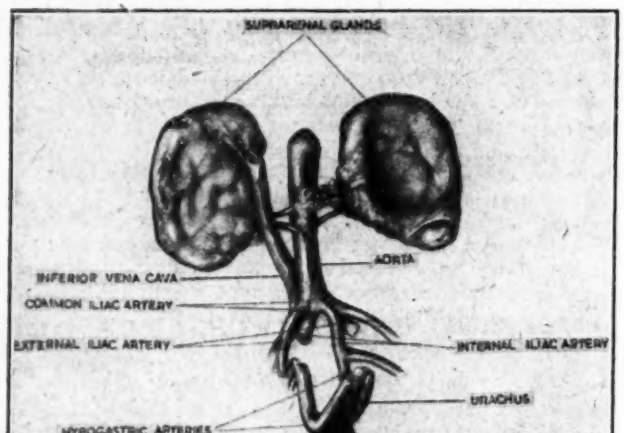
Case 1

The mother, aged 40 years, had four previous normal pregnancies. The last child, aged 6 years, had an undescended right testicle. The other children, one boy and two girls, were normal and healthy. There was no history of congenital deformity in either the mother's or the father's family.

The early antenatal period appeared normal, although the mother later admitted that six weeks after the last menstrual period she had taken about 2.3 g. (35 gr.) of a quinine salt in one day, followed by 85 ml. (3 fl. oz.) of an ergot mixture and two tablets of an unknown substance.

At the 35th week she was admitted to hospital with antepartum haemorrhage due to placenta praevia. The foetus presented by the breech, and the foetal heart was strong and regular. Two weeks later a lower-segment caesarean section became necessary because of severe haemorrhage. The placenta was lying centrally in the lower uterine segment, and it was noted that the liquor amnii was normal in amount.

The child, a boy weighing 2,920 g. (6 lb. 7 oz.), showed a lax skin, generalized cyanosis, and hypotonia. The skull was scaphoid, with a tense anterior fontanelle and an occipito-frontal circumference of 37 cm. (14½ in.). A misshapen left pinna was noted. No abnormality was detected in the cardiovascular, alimentary, or central nervous systems. Rapid grunting respirations, with marked intercostal and subcostal recession and scattered crepitations, persisted throughout life, which lasted 20 hours and 40 minutes.



A dissection from the anterior aspect. The kidneys and renal arteries are absent. Discoid suprarenals are shown.

Necropsy revealed no abnormalities in the brain, thyroid, thymus, heart, spleen, liver, pancreas, and gastro-intestinal tract. A haemorrhagic consolidation was present in the posterior aspects of both lungs, and aeration was present in their anterior margins.

The adrenals were discoid, and measured 4.5 cm. by 3 cm. (see Diagram). There was complete absence of both kidneys, renal arteries, and ureters. A small prostate and bladder were present. Complete descent of the testes had taken place. The penile urethra was patent in the terminal 0.5 cm. A microscopical search for renal tissue failed to reveal its presence.

Cases 2–4

Three other cases of anephrogenesis were discovered in the records of the West Middlesex Hospital. In Tables I, II, and III the details available are summarized and are compared with those of the case described above.

TABLE I.—*Summary of Pregnancies*

Case	Age		Month of Conception	Parity	Abnormality of Pregnancy	Maternal Health	Amount of Liquor
	Mother	Father					
1	40	46	February	4	1. Breech 2. Placenta praevia	Good	Normal
2	18	21	August	0	Mild toxaemia	Good	No record
3	45	?	September?	5	None	Mitral and pulmonary systolic murmurs	Very little
4	25	52	February	0	Mild toxaemia	Diffuse enlargement of thyroid for many years	No record

TABLE II.—*Summary of the Infant Data Prior to Death*

Case	Duration of Pregnancy in Weeks	Birth Weight	Sex	Weight of Placenta	Duration of Life
1	36	6 lb. 7 oz. (2,920 g.)	M	1 lb. 3 oz. (548 g.)	20 hr. 40 min.
2	34	3 lb. 13 oz. (1,730 g.)	F	12½ oz. (354 g.)	2 hr. 20 min.
3	34	4 lb. 14 oz. (2,210 g.)	M	No record	28 hr. 30 min.
4	40	5 lb. 12 oz. (2,608 g.)	M	9 oz. (255 g.)	Stillborn

Aetiology

The present knowledge of the aetiology of congenital abnormalities is reviewed fully by Warkany (1947) and Fraser and Fainstat (1951). The two main groups are: (1) genetic and (2) environmental. The latter includes nutritional deficiencies and chemical, physical, endocrine, infectious, and mechanical agents. The timing of the environmental disturbance has been shown experimentally by Ingalls *et al.* (1950) to be important in deciding the site and nature of a congenital defect. These factors are applicable to congenital deformities of the renal tract.

Arey's (1946) calendar of human development shows that by the fourth week of embryonic life the pronephros has

TABLE III.—*Clinical and Pathological Findings*

Case:	1	2	3	4
Head	Scaphoid skull; misshapen left ear	Asymmetrical	Considerable head moulding; bilateral accessory auditory auricles	Dolichocephaly; cranial bones friable and thickened
Respiratory system	Cyanosis; congenital atelectasis	Cyanosis; congenital atelectasis	Cyanosis; congenital atelectasis	Bilateral pulmonary hypoplasia
Cardiovascular system	No abnormality	No abnormality	No abnormality	Patent interventricular septum
Alimentary system	No abnormality	No abnormality	Intestinal adhesions; ectopic caecum	"Hour-glass" constriction of stomach
Locomotor system	No abnormality	Limited flexion and abduction of both hips; hypermobility of right knee	No abnormality	Deformed hands and feet; limbs splinted against trunk
Urogenital system	Absence of both kidneys and ureters; rudimentary bladder	Absence of both kidneys and ureters; failure of fusion of Müllerian ducts; bladder elongated	Absence of both kidneys and ureters; small bladder	Absence of both kidneys and ureters; bladder present

reached maturity and begun to degenerate. Between the fourth and sixth weeks the mesonephros, mesonephric duct, ureteric bud, and metanephros are undergoing active developments. The future of the kidney depends upon: (1) the successful caudal migration of the mesonephric duct; (2) the sprouting of the ureteric bud; (3) the formation of the metanephros; and (4) a combination of these three processes. The "critical period" of renal formation is between the fourth and sixth weeks of intrauterine life, and it is during this period that one would expect noxious environmental influences to be most effective.

Discussion

It is suggested that Case 1 is an example of congenital abnormality caused by disturbed environment. Six weeks after her last menstrual period, in a regular cycle of 6/27, the mother swallowed 2.3 g. (35 gr.) of a quinine salt within 24 hours, and later 85 ml. (3 fl. oz.) of an ergot mixture and two tablets of an unknown substance. The probable age of the embryo at this time—4 to 6 weeks—covered the important developmental periods of the mesonephric duct, cloaca and ureteric bud.

Quinine salts are known to be protoplasmic poisons with a specific nephrotoxic action. They are readily absorbed into the blood stream, and Dilling and Gemmell (1929) showed that quinine crosses the placental barrier at term. Huggett and Hammond (1952) state that placental permeability of different agents varies according to the stage of development. We have been unable to trace experimental proof that quinine reaches the human ovum from the maternal blood in the first few weeks of pregnancy. However, we submit that it is not unreasonable to regard quinine as the agent responsible for the agenesis of the kidneys in Case 1. Our assumption is that the drug acted direct on the rapidly differentiating renal tissue.

The deformity of the left pinna is interesting. Potter noted certain facial characteristics, which included large low-lying ears with cartilaginous dysplasia. In a six-weeks embryo the external ear is beginning development around the first branchial cleft. Therefore it may be supposed that disordered differentiation of the tissues at this time was the result of an insult, the timing of which coincided with the quinine administration.

One weakness in our hypothesis is the fact that quinine and other drugs are often taken as abortifacient measures during the early weeks of pregnancy and yet bilateral anephrogenesis is rare. There are three points to make in reply. First, the drug must be taken at the correct time in the development of the renal tract; the margin of error in time allowance is probably very small. Secondly, it is necessary to assess the incidence of anephrogenesis in the embryos and foetuses of abortions. Thirdly, the dosage and concentration of the drug must be sufficiently great.

Summary

Four cases of congenital absence of both kidneys are reported. One of these cases is described in detail.

The aetiology of the condition is discussed. The fourth to sixth weeks of embryonic life are the "critical period" during which development of the kidneys is taking place, and is the time when noxious environmental factors could exert their most damaging effects.

Quinine, taken by the mother of one case in a large dose six weeks after her last menstrual period, is suggested as a possible cause of the renal agenesis.

We wish to thank Dr. M. Dynski-Klein, Mr. D. M. Stern, and Miss I. M. Titcomb for allowing us to report these cases under their care and for access to their records; Dr. A. C. Counsell for his careful pathological examinations; and Miss S. Robinson for the drawing.

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USE OF UNSATURATED FATTY ACIDS IN THE ECZEMAS OF CHILDHOOD

BY

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Burr and Burr (1929, 1930) and Burr *et al.* (1932) showed that the total exclusion of fats from the diet of young rats produced a deficiency disease with caudal necrosis, red and somewhat swollen feet, and scaliness in the hair of the back. At the same time the growth of the animals was arrested and there was much loss of weight. This condition was not improved by adding non-saponifiable fats to the diet, but was cured by the unsaturated fatty acids (U.F.A.s), particularly linoleic and linolenic acids.

This work stimulated Hansen (1933), who first made the suggestion that U.F.A.s might be useful in treating infantile eczema. He demonstrated that there was a diminution of these acids in the serum of eczematous children, and he claimed that the addition of U.F.A.s to their diet caused a clinical improvement which was associated with a rise in the iodine number, an index of the non-saturated fatty acids in the serum. Shortly afterwards Cornbleet (1935) reported good results in a series of 85 cases of eczema which had been treated with fresh lard by mouth, but there seems to be no reference to any control in his investigation. Taub and Zakon (1935) found no benefit in eight cases of atopic eczema (Besnier's prurigo, disseminated neurodermatitis) which they treated with linseed oil by mouth, and also pointed out that the use of linseed or cottonseed oil might be dangerous, as the patient could be sensitive to these sources of U.F.A.s. Ginsberg and Bernstein (1937) found satisfactory improvement in three adults in a group of 11 with atopic dermatitis and in four out of six children. They also pointed out, however, that two children receiving the same local treatment and no added U.F.A.s improved in the same time. Finnerud, Kesler, and Weise (1941), using fresh lard in older children and adults, had a satisfactory response in about half their cases. Hansen, Knott, *et al.* (1947) reported on the study of 225 cases of eczema, of whom 123 were under the age of 2 years, 67 were from 2 to 15, and 35 were 16 and over. During these trials they used many forms of local treatment, including boric acid, zinc paste, sulphur, resorcinol, and occasionally coal-tar. Their results were poor in only 37 of the 148 cases treated with supplementary fatty acids, while 18 of the 48 controls were unsatisfactory in the same

period. They also demonstrated that the iodine number is reduced in many cases of eczema and returns to normal on satisfactory treatment.

More recently European workers have stepped into this field with investigations and reports on lines similar to those of the earlier American articles. As early as 1942 Justin-Besançon and Laroche criticized those who saw fit to call linoleic acid "vitamin F," and also pointed out that the administration of U.F.A.s gave very divergent results and that "the conclusion that certain authors wish to draw seems insecurely based." Azerad and Grupper (1949a) summed up their experience and claimed that lard by mouth was giving extremely encouraging results, but later (1949b) they reported better results with purified linoleic acid. In 58 breast-fed infants, 18 children, and 24 adults whom they treated they obtained 52 excellent or good results, and only 17 were mediocre or negligible. It must be pointed out that the linoleic acid was only a supplementary form of treatment, and as local treatment they used "nothing except a paste or ointment of 10% tar," which they deliberately chose in view of the excellent action of tar on vesicular and weeping eczema. Touraine (1949) quotes Pätiälä (1948), who found an improvement in infantile eczema treated with vitamin B_6; and Charpy (1948) combined this with the U.F.A.s and claimed there was a synergistic effect, but Hansen was unable to confirm this. Touraine also quotes Vachon (1948) as having tried the application of 3% linoleic acid in an ointment base, which was found to irritate, and he used a 1% ointment in resistant cases but said it should be employed with care. Alechinsky (1950) claimed six complete cures in 11 cases, while Dubois (1950), summing up the Continental view, pointed out that local treatment, preferably tar, was indispensable and claimed that irritation ceased in four to seven days and exudation dried in two to four days. More recently Finzi (1951) and Carletti and Scalamogna (1952) claimed good results, but in an apparently uncontrolled series of cases.

The unsatisfactory state of these claims and the associated recent publicity in this country of the use of unsaturated fatty acids, particularly linoleic and linolenic acids in liquid, ointment, and capsule form, suggested that an investigation of their effectiveness should be undertaken.

The following investigations were therefore carried out at a hospital mainly for the long-term treatment of children with severe and chronic dermatoses.

Local Application and Oral Administration of U.F.A.s

For the first investigation 27 cases of infantile and atopic eczema were used. The ages ranged from 18 months to 15 years, and so far as was possible the cases were paired in age and type of skin lesion. The babies with infantile eczema had usually been in hospital only a short time, while most of the older children had spent a considerable period in hospital. As a result of this long-term treatment any improvement which might have been attributed to the child's change of environment on admission to hospital was, in the main, avoided.

Each child was seen at the start of the trial and assessed, and after that, without the investigator's knowledge of which children were being treated, 15 children were given a daily application of an ointment with the following formula:

Linoleic acid	1.7%
Linolenic acid	0.8%
Hydrous ointment .. .. to	100%

and orally a capsule a day:

Linoleic acid	0.27 g.
Linolenic acid	0.13 g.
Arachis oil .. .. .. to	0.5 g.

The other 12 children continued the routine treatment of the hospital, usually zinc ointment with boric acid and various strengths of tar. An independent dermatologist (Dr. G. B. Dowling) also saw the patients regularly, and if the child's condition deteriorated enough to warrant a change of treatment the case was automatically graded as −2. Each child was seen and assessed weekly, and at the end of seven weeks the progress was marked in the following way:

Improvement amounting almost to cure	+2
Overall improvement	+1
Approximately the same as at the start	0
Overall deterioration	−1
Failure, needing change of treatment	−2

It was not until all these cases were marked that the investigator knew which patients were being treated with the U.F.A.s. In that way any bias for or against the treatment was avoided.

The results (Table I) showed no evidence that the treatment with local and oral unsaturated fatty acids was a satisfactory substitute for the normal routine. The possibility

TABLE I

	+2	+1	0	−1	−2	Total
Cases on local and oral U.F.A.s	1	0	1	8	5	15
Cases on usual treatment ..	3	5	2	1	1	12

that the ointment itself might irritate was considered, but the fact that one child steadily improved while on the treatment disproved this. Later, at the end of the series, patch tests with the ointment were made in cases that had failed, but no evidence of sensitivity to the ointment was found. It was thought that this group of cases showed striking evidence against the further continuation of the trial, but in order to assess whether oral U.F.A.s in addition to the routine hospital treatment was of benefit a further investigation was made.

Oral U.F.A.s as an Adjuvant to Therapy

This group consisted of 36 cases of infantile eczema and atopic eczema, 20 of whom took a capsule of linoleic and linolenic acid daily for approximately four months. The actual time that patients were treated varied from nine to seventeen weeks. Several of the children were discharged from hospital in this time and they were automatically marked +2. Again any child whose treatment was altered because of manifest deterioration was graded −2.

TABLE II

	+2	+1	0	−1	−2	Total
Routine treatment plus oral U.F.A.	7	8	3	2	0	20
Routine treatment	8	3	3	1	1	16

Taking into consideration the slightly smaller group of controls, it is not considered that this investigation produced any evidence that oral U.F.A.s have value as an adjunct to local treatment of infantile or atopic eczema.

Discussion

The diminution of the iodine number showing the reduction of U.F.A.s in the serum of children with eczema caused Hansen to start this long and contradictory series of investigations. The conception that a reduction in the U.F.A.s of the serum is aetiologically connected with infantile eczema was doubted by Faber and Roberts (1933), who found that in eczema the cholesterol was slightly higher, the total fatty acid and the total lipid content considerably higher, and an iodine number only moderately lower than in normal controls. They did not find a degree of unsaturation as high as Hansen did, and expressed a belief that the findings were secondary rather than causative. This suggestion would seem to receive support from Hansen's own work, which shows there is a rise in the iodine number in children satisfactorily treated for eczema with nothing but local applications of tar (Hansen, 1933; Hansen, Knott, *et al.*, 1947).

The emphasis placed by nearly all authors who claim benefit from the use of these fatty acids on the fact that

local treatment is a prime necessity, and the apparent lack of any great interest in a controlled series, suggest that the benefits claimed may be due to the usual treatment, with perhaps a dash of enthusiasm.

The investigations reported here, in which all personal bias and normally varying factors were removed so far as was possible, have failed to substantiate the claims that the so-called "vitamin F" has any value in the treatment of atopic and infantile eczema. The findings of Vachon seem to be borne out, in that the ointment almost invariably irritated the eczematous skin.

Summary

A brief summary of the literature on the use of unsaturated fatty acids in the treatment of infantile and atopic eczema is followed by the details of a recent investigation.

The combined use of linoleic and linolenic acid ointment and capsules and the use of the capsules as an adjuvant to routine treatment were in no way preferable to the established methods of treatment.

My thanks are due to Dr. G. B. Dowling for allowing me to see and investigate his cases, and to the matron and nursing staff of the Goldie Leigh Hospital for their willing co-operation.

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Medical Memoranda

Total Gastrectomy for Haematemesis

The object of this report is to point out the necessity for total gastrectomy in certain rare cases of haematemesis and to stress the value of oesophagoscopy in diagnosing the source of the haemorrhage.

Obvious bleeding occurs in some 20% of all peptic ulcers, and these form about 85% of all cases of haematemesis and melaena. The total mortality rate in the peptic ulcer group is roughly 8%, but in patients under 45 it is 2%. Death more often takes place from irreversible changes following prolonged anoxia than from acute anaemia, as necropsy nearly always shows the vessel occluded by clot. Hence the sheet anchor of treatment is blood transfusion, not only to prevent anoxia but also to enable the patient to withstand further haemorrhage by keeping the haemoglobin level about 80%. If this rule is followed the so-called critical periods on the third day or at any other time cease to exist, and surgery is indicated when replacement does not control the loss or if the loss continues or recurs for several days.

HAEMORRHAGE FROM FUNDUS OF STOMACH AND LOWER OESOPHAGUS

The importance of haemorrhage from the fundus of the stomach was first impressed upon me by a patient, known to be suffering from a chronic gastric ulcer for some years, who was admitted with severe haematemesis which did not respond satisfactorily to transfusion. A partial gastrectomy was successful, but the specimen showed that the bleeding was not from the known chronic ulcer but from a small acute ulcer high up the lesser curvature which had been included in the resected area by luck, not judgment. This acute ulcer was not palpable to the gloved finger, and I doubt if it would have been noticed on gastrotomy, which in other cases has proved to be of no value.

Further, the importance to the differential diagnosis of the site of the haemorrhage was brought home by another man, known to have a chronic gastric ulcer, who was admitted with severe haematemesis not controlled by transfusion. At partial gastrectomy cirrhosis of the liver was noted. He died five days later from continued bleeding from oesophageal varices. No evidence of haemorrhage from the ulcer was found. This error might have been prevented by an oesophagoscopic examination, in which it is simple to distinguish a normal oesophagus, a normal oesophagus with regurgitated blood in it, bleeding oesophageal varices, or a stomach distended by gastric haemorrhage. In fact, since then it has saved me from making the same mistake again.

Those who are not trained in the use of the common instruments for the visualization of their patients' orifices will find no difficulty in passing an appropriate-sized oesophagoscope if they will first pass a stomach tube, aspirate, and then pass the endoscope alongside it before its removal.

Treatment.—This must be governed by the general principles already mentioned. When surgery is indicated for gastric haemorrhage from acute ulceration it is no use temporizing by doing a gastro-enterostomy (as in my house-surgeon days) or a partial gastrectomy or ligation of gastric vessels (as is often done now). I know of deaths from continuing haemorrhage after these procedures have been carried out by competent surgeons and also of recovery when nothing has been done. Acute fundic ulceration is probably as common as is acute ulceration in any other part of the stomach, and unless at laparotomy the surgeon can determine the site of bleeding he is faced with only two logical procedures: nothing or total gastrectomy. The following case histories illustrate the problem.

CASE 1

An engineer aged 58 collapsed at work on March 16, 1952, and was admitted to Lodge Moor Hospital the next day as a case of "influenzal pneumonia." No cause for his collapse was found on admission, but 48 hours later he had a severe haematemesis. Blood transfusion was at once started, and he was transferred later in the day (March 19) to the City General Hospital. His pulse was 130 and blood pressure 105/60, and he was pale, cold, and clammy. Further transfusion was given, with improvement.

On March 21 he had further haematemesis and melaena in spite of a total of 8 pints (4.5 litres) of blood, so I was asked to see him with a view to surgery. His pulse was 84, blood pressure 85/55, Hb 8.8 g. (60%). He gave a history of several weeks of epigastric discomfort after food lasting an hour or so, and then complete freedom for several days before the next recurrence. I felt that the diagnosis of a chronic ulcer or carcinoma was very unlikely and suggested further conservative treatment.

However, on March 26 his condition deteriorated in spite of a total of 21 pints (11.9 litres) of blood, and laparotomy was advised.

First Operation.—On March 26, under intratracheal gas and oxygen, thiopentone, and D-tubocurarine chloride, a left upper paramedian incision was made. External exploration of the stomach and duodenum showed no lesion or evidence of scarring from an old lesion. The intestines were full of blood. The anterior stomach wall was incised from the lesser to the greater curvature roughly at its mid-point and the contents were aspirated. No fresh blood was present, but some adherent clot at the fundus was found. Nothing abnormal was seen or palpated though ungloved hands were used. The lower oesophagus also felt normal. The problem was total gastrectomy or nothing, and I chose the latter

course in the hope that the gastric haemorrhage, which was presumed to have come from the fundus, where adherent clot was found, would not recur.

The patient's condition improved for several days, though intermittent melaena occurred. On April 1 I passed an oesophagoscope into the stomach and found no evidence of bleeding or lesion in the oesophagus, but there was old clot in the stomach. Shortly after this he started to bleed severely, and as the consulting haematologist again found no evidence of blood dyscrasia I decided to do a total gastrectomy.

Second Operation.—On April 1, under a similar anaesthetic, the old incision was opened up and extended. There was a good deal of mild peritonitis due to the previous gastrotomy. Total gastrectomy was performed and a retrocolic jejunal loop was anastomosed to the oesophagus without entero-anastomosis (operative time two hours).

Recovery was uneventful and the patient was discharged on April 26 on an unrestricted diet. He had received 52½ pints (29.8 litres) of blood from March 19 to April 2. He was readmitted on February 3, 1953, with acute intestinal obstruction for which section of a solitary cord adhesion from the mesentery to the posterior abdominal wall was done. In June he was at work again, the blood counts, etc., being satisfactory.

Specimen.—The stomach showed about a dozen small erosions, three or four being in the pyloric region and the rest on the posterior wall of that part opposite to and above the oesophageal opening. The haemorrhage had occurred from the largest of these fundic lesions, which measured about 1 cm. in length and 2–3 mm. in width.

CASE 2

A crane-driver aged 48 was admitted to the City General Hospital on June 27, 1952, with severe haematemesis. His history was as follows: 1930, onset of symptoms of duodenal ulcer; 1941, pyloric obstruction—gastro-jejunostomy; 1947, severe haematemesis—14 pints (8 litres) blood transfused; 1950, further haematemesis—3½ pints (2 litres) blood transfused; 1951, high partial gastrectomy for two anastomotic ulcers. I first saw him at 9 p.m., after he had vomited 38 oz. (1 litre) of blood. His condition was improving under transfusion. The Hb was 62.5%, but, as it fell to 55% in the next twelve hours in spite of drip transfusion, I decided to operate without further delay though the rate of transfusion was increased.

Operation.—On March 28, under gas and oxygen, thiopentone, and D-tubocurarine anaesthesia, oesophagoscopy was carried out. The oesophagus was normal, but there was blood in the stomach. A left postero-lateral thoracotomy was done with resection of the eighth rib. Total gastrectomy was performed with considerable difficulty in 3 hours 10 minutes. Unfortunately, the patient died some 30 hours later, but the cause of the haemorrhage was acute ulceration of the fundus of the stomach.

JUDSON T. CHESTERMAN, F.R.C.S., F.A.C.S., M.R.C.P.

Two Cases of Ovarian Cyst in Childhood

The deceptive presentation of these cases—one as retention of urine and the other as appendicitis—is of clinical interest.

CASE 1

In October, 1950, a girl aged 3½ was admitted to hospital with acute retention of urine. A week previously she had had a sore throat and diarrhoea with much mucus in the stools; this cleared up after three days, but two days later she began to have frequency, and micturition was apparently difficult and painful. The urinary symptoms increased in severity and culminated in acute retention.

On examination of the abdomen a smooth rounded cystic swelling was found rising out of the pelvis half-way up to the umbilicus. This was taken to be the distended bladder. The external urethral orifice appeared normal, there was no fever or any evidence of a neurological lesion, and an *x*-ray film of the abdomen and pelvis showed nothing abnormal. With difficulty a catheter was passed and only a few millilitres of normal urine was obtained.

Under a general anaesthetic the cystic swelling previously described, which had been mistaken for the urinary bladder, became disimpacted from the pelvis, and at a subsequent laparotomy was shown to be a large multilocular teratoma of the left ovary, measuring 11 by 6.5 cm. It was removed without difficulty.

The mechanism of the production of urinary retention was possibly the same as that which occurs in retroflexion of the gravid uterus, whereby the urethra is compressed and elongated. The bladder, normally an abdominal viscus in young children, is easily displaced and compressed anteriorly by the impacted ovarian cyst. Disimpaction under anaesthesia allowed the bladder to empty easily and no further dysuria was experienced. Urinary disturbances occur not uncommonly in cases of ovarian cyst in children, but the occurrence of acute retention seems to be quite rare.

CASE 2

In June, 1951, a girl of 4 years 9 months was admitted to hospital with abdominal pain and vomiting. She had had three attacks of constipation and abdominal pain lasting two to three days in the past nine months. The present attack began three days before admission, with vomiting and lower abdominal pain. She had been constipated for three days and had been irritable and had a poor appetite. There were no urinary symptoms.

On examination she was seen to be flushed, with mild pyrexia and tachycardia. There was a tender rounded swelling arising out of the pelvis and extending 2 in. (5 cm.) above the symphysis pubis; slight muscular guarding was present over it. Rectal examination revealed a tender swelling palpable through the anterior wall of the rectum. A catheter was passed readily and 2 oz. (57 ml.) of urine was withdrawn. A diagnosis of pelvic abscess or cyst was made. Under general anaesthesia the swelling emerged from the pelvis and was freely mobile in the abdomen; it was evidently a cyst. The subsequent laparotomy revealed a right-sided unilocular ovarian cyst which had undergone torsion twice in a clockwise direction. It was removed. The left tube, the ovary, and the uterus were normal. Convalescence was uneventful, and the patient was discharged on the eighth day. On section a simple ovarian cyst with haemorrhage into the ovary was reported.

COMMENT

Study of reported cases shows that simple or multilocular cysts of the ovary account for one-quarter to one-third of all ovarian neoplasms in girls under 15 years, while granulosa-cell tumours produce symptoms of precocious puberty, and teratomas can sometimes be recognized by *x*-ray examination; ovarian cysts may remain unrecognized for a long time. Lower abdominal pain, distension, constipation, and frequency may occur. Torsion leading to acute symptoms may be the first indication of the presence of an ovarian cyst, and differential diagnosis from acute appendicitis may be very difficult; in fact, many series of reported cases show that this is the commonest pre-operative diagnosis, particularly as most cysts are on the right side. Steel (1931) reported 25 cases of twisted ovarian cysts diagnosed pre-operatively as appendicitis.

The most useful procedure to help in diagnosis is probably rectal examination, this fact being emphasized in many reports; it was of great assistance in these cases.

We are indebted to the late Mr. J. O. D. Wade, Professor A. G. Watkins, and Mr. R. J. Williams for permission to publish these cases.

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Reviews

CLINICAL GENETICS

Clinical Genetics. Edited by Professor Arnold Sorsby. 31 Contributors. (Pp. 580+23; 311 illustrations. 90s.) London: Butterworth and Co. 1953.

The plan of this book is both novel and excellent. No space is wasted in providing what must perforce be, within any reasonable limits of length, an inadequate account of the principles of general and human genetics. It is assumed that the reader is already familiar with these, and so the first quarter of the book comprises just what such a reader would probably like to turn to next—namely, a series of more advanced essays on subjects of interest and importance relevant to the medical field. The twelve essays are very good indeed, and it may be invidious to single out particular chapters for special note; but, taking that risk, we might mention Neel on the detection of carriers of inherited disease, Mather on polygenic inheritance, Koller on cytogenetics, and Catcheside on chemical genetics; they have written the kind of contribution which is possible only when the author is discussing a subject of which he is master and when he has taken pains to make the presentation as concise and as clear as is reasonably possible.

The rest of the book is called clinical and covers the genetics of the various systems and specialisms. The whole field is covered, but naturally within the space of a single volume there must be compression, whether by omission of less important topics, or even more by rather brief summaries of what is known about some inherited conditions. Editorial difficulties must have been considerable, and there is indeed some lack of balance in the result. It is reasonable enough to compress the chapter on ophthalmology in view of Sorsby's own recent book, and a similar shortening is understandable with mental deficiency, for which subject Penrose's *Biology of Mental Defect* is available, and again in dermatology, where Cockayne's *tour de force*, although twenty years old, is still invaluable. But why should 26 pages be devoted to the alimentary system, with only six conditions to describe, and no more than 23 to the host of neurological disorders, for which there is no genetic textbook? Incidentally, both are excellent chapters, but, whereas Carter is able to marshall the evidence at leisure, Pratt has to discuss some conditions in briefest summary and omit a number altogether.

The one real failure of the book is in the bibliographies. To anyone specially interested in a particular condition the most that a single volume can provide, and what indeed this volume usually does provide, is a relatively brief, accurate, and up-to-date summing-up. The essential accompaniment is a carefully selected bibliography which will guide the inquirer to the key references. The bibliographies of this book are most uneven. Some are excellent, with the more important references specially indicated, but many are impossibly brief. Sometimes papers are quoted in the text to which there are no references in the bibliographies. Sometimes references are given to papers which are not discussed. Some authors quote the titles of the papers while others do not. It is a pity that the usefulness to the research worker of so excellent an undertaking should have been diminished by neglect of such an important point.

Once again the gremlins have been busy over genetic linkage. There is a reference to two conditions being possibly linked because they tend to occur together, an unfortunate lapse in a book in which a special chapter is devoted to the subject. The best human example for demonstrating the workings of genetic linkage is haemophilia and colour-blindness, and the reader is duly shown in Fig. 206 a pedigree in which the two genes are in repulsion, that is, in opposite chromosomes, followed by a pedigree in which they are in coupling. Then comes Fig. 207, stated to show an example of crossing-over. But, alas, it shows nothing of the kind, for Riddell's original pedigree has been wrongly reproduced.

The book is beautifully illustrated and produced and should prove of great value to a variety of readers. But the second edition should be considerably more valuable, for then, it may be hoped, balance will be improved, errors removed, and, above all, adequate bibliographies provided.

J. A. FRASER ROBERTS.

CELL STRUCTURE AND FUNCTION

Histology. By Professor Arthur W. Ham, M.B., F.R.S.C. Second edition. (Pp. 846; 518 figure numbers, including 7 plates in colour. 80s.) J. B. Lippincott Company. 1953.

An Introduction to Functional Histology. By Geoffrey Bourne, D.Sc., D.Phil. (Pp. 188. 98 illustrations. 21s.) London: J. and A. Churchill, Ltd. 1953.

These two books have, as a common objective, the correlation of the dull subject matter of purely descriptive histology with cell, tissue, and organ function. They are primarily designed for the use of undergraduates. Both are written in clear, vivid, and unambiguous language, easily understandable by the average student, and in spite of its complexities both authors have tackled their problem with commendable success.

This is the second edition of Professor Ham's book, which is a full and comprehensive treatise on microscopic anatomy, greatly simplified by the generous use of excellent photomicrographs and clear diagrams. The bare facts of normal structure are skilfully blended with those of biochemistry, physiology, and the principles of pathology. Both structural and functional sides are up to date, and the author includes much new knowledge on such subjects as cytoplasmic nucleic acid, chromosomal structure, the function of mitochondria, submicroscopic particulates, and electron microscopy.

Professor Ham, who was a pathologist before he became a histologist, has taken every opportunity to introduce enough histopathology to help the student in correlating normal structure with common pathological processes. An outstanding chapter on the normal structure of bone, for instance, is followed by an account of fracture healing and the fate of a bone graft; an account of tissue fluid, by a discussion on oedema; the structure and functions of the skin, by a simple account of burns and skin grafting; and those readers remembering the author's many contributions to cancer research will welcome several reliable and stimulating accounts of the general characteristics of the malignant cell included in the chapters on cytology.

Dr. Bourne's slim volume must in these days of rapid biological progress be regarded as an essential companion to any purely descriptive treatise on normal histology. To the best of the reviewer's knowledge this is the only book suitable for undergraduate readers which has seriously attempted and brilliantly succeeded in bringing together the results of recent cytological research and blending them with modern physiology. A chapter on histochemical technique, with special reference to the identification of cell and tissue enzymes, will prove of immense value to students who are seriously attracted to the subject and wish to satisfy themselves of the reality of modern intracellular enzymology. We confidently predict that the author's refreshing approach will strongly appeal to all students of general biology.

GEOFFREY HADFIELD.

MANUAL OF PSYCHOLOGICAL MEDICINE

Manual of Psychological Medicine for Practitioners and Students. By A. F. Tredgold, M.D., F.R.C.P., F.R.C.S., and R. F. Tredgold, M.A., D.M., D.P.H. Third edition. (Pp. 328. £1 5s.) London: Baillière, Tindall and Cox. 1953.

Relatively few recent textbooks of psychiatry are free from some sort of aetiological bias, and most of those from the U.S.A. can be labelled as belonging to one school of thought or another. A thoroughly orthodox British descriptive psychiatry is therefore much needed. The third edition of "Tredgold" covers an even wider field than its

predecessors and it has been brought up to date so far as facts are concerned. The attitude to mental maladjustment lacks the therapeutic optimism of the present generation, and, while rejecting as false the gods of psycho-analysis, the authors have tried to do without any very consistent theme at all. The result is a competent compilation in which the different clinical entities are described in detail according to their importance in practice. This will meet the immediate needs of the student and the practitioner, but does not give him much chance to build up a frame of reference into which facts from other sources can later be fitted. This is especially true of the discussion of treatment, where enough is usually given to satisfy an examiner who does not inquire too closely, but it is not the sort of information which helps to avoid pitfalls in treating a patient.

On the other hand, the description of types of neurotic maladjustment which actually come to the consulting-room are most realistic, especially when the minor degrees of instability, psychopathy, and inadequacy are under consideration. Terms such as neurasthenia and eccentric paranoia are made to justify themselves; the section on malingering contains a wealth of experience; while the section on war neuroses extracts in a few pages the more important lessons of the recent conflict.

It is to be recommended as a thoroughly safe textbook.

ALEXANDER KENNEDY.

THE ELDERLY SICK

The Nursing of the Elderly Sick: A Practical Handbook of Geriatric Nursing. By T. N. Rudd, M.D., M.R.C.P. (Pp. 108. 8s. 6d.) London: Faber and Faber. 1953.

This is not a mere textbook of nursing for the elderly: it is far more than that. The writer has a humane and eminently sane approach to a problem which is steadily growing as the expectation of life increases. He appreciates the fact that the first essential to success in this field is to understand the working of the elderly mind, to enter into its fear of being useless or unwanted, to understand that horror of crippling is far greater than the dread of death.

It is interesting to read that only half of the old for whom hospital treatment is sought require medical or nursing treatment which could not be provided at home. The difficulty is to secure adequate supervision at home now that whole families go out to work. In the more leisurely days, before emancipation of women, it was the lot of the unmarried daughters to tend their aged and sick parents. This abominable servitude has fortunately been swept away by economic necessity; something better must be found to replace it. Homes for the aged are a crying need. The author stresses the fact that senile dementia is more likely to be the result of environment than of organic disease: loneliness and boredom are the evil influences.

The sections on incontinence, nutrition, bed sores, and diet are highly practical, and should be of great help to doctors and nurses in caring for the sick of all ages.

A. H. DOUTHWAITE.

MEDICAL MYCOLOGY

Atlas of Medical Mycology. By Emma Sadler Moss, M.D., and Albert Louis McQuown, M.D. (Pp. 246; 248 illustrations. £3 1s. 6d.) London: Baillière, Tindall and Cox. 1953.

This atlas is based on wide practical experience of mycotic infections in New Orleans. Its aim is to facilitate the identification of pathogenic fungi and the histological diagnosis of the diseases they produce. The authors present about 250 photographs in the style of the introductory manual of medical mycology by Lewis and Hopper. But they discuss the subject more uniformly and without the same emphasis on skin and dermatophyte infections.

The descriptive text is a concise and practical elementary summary representing generally accepted present-day teaching. A chapter on immunology is inadequate, and the use of the term "vaccine" for skin-testing antigen is likely to cause confusion. The debatable nature of pulmonary moniliasis might perhaps have been considered, and the importance of *Aspergillus fumigatus* might have been mentioned under the pathogenic aspergilli. There are some inconsistencies in the use of capitals for specific names of fungi, and the choice of chromomycosis in preference to the more generally accepted name, chromoblastomycosis, is unusual. In discussing technical methods it is clear that the authors are impressed by the results of primary isolation of pathogenic fungi on Littman's bile-salt crystal-violet streptomycin medium. Consequently it is given considerable prominence among media more generally used. This recommendation merits attention and confirmation. The appearance of cultures under ultra-violet light is described in greater detail than is warranted for normal routine diagnosis.

It is unfortunate that the quality and usefulness of the illustrations vary widely. Many of those depicting cultures serve no useful diagnostic purpose and scales are applied without care. The detail demanded from a number of photographs has not been realized, and microscopical fields of fungous cultures could have been chosen with more discrimination. There is a brief and unusually varied bibliography, but no reference is given to it in the text.

R. W. RIDDELL.

FOOD HYGIENE

Food Poisoning and Food Hygiene. By Betty C. Hobbs, B.Sc., Ph.D., Dip.Bact. (Pp. 174: 44 figures. 14s.) London: Edward Arnold and Co. 1953.

Food-poisoning has reached alarming proportions in recent years. One of the major causes is the increasing tendency to take meals in canteens and restaurants, where methods of preparing and serving food by mass production provide the mechanism for extensive outbreaks if technique is faulty. The danger to health is incalculable; the effect on human endeavour can be chaotic. An outbreak of dysentery in a hospital upsets routine, restricts admissions, and slows the tempo of the institution; the introduction and spread of infection in day and residential nurseries occur frequently, impairing their usefulness and on occasion dictating their closure for a time; widespread food-poisoning in a works canteen cripples production, with consequent loss of wages and profits. Too little attention has been paid to this serious problem of public health and national economy.

Dr. Hobbs has used her opportunities and experience as director of the food hygiene laboratory of the Central Public Health Laboratory to great advantage. She presents the facts of food-poisoning and the remedies of food hygiene simply and authoritatively. She demonstrates disturbingly the high rate of increase of infection over a period of years, although it is but right to point out that the high efficiency of the Public Health Laboratory Service is undoubtedly one cause of higher figures in that ascertainment is much improved.

But Horace's Homer nodded, and here the statement on the cover that "the number of notified outbreaks of food poisoning during the last ten years has increased at almost exactly the same rate as the number of catering establishments" must be challenged. The increase is quite definite, but the rate of increase is not nearly the same. Furthermore, a graph which appears at first sight to support the statement is found to be of unsound construction in that the vertical scale is not consistent, and the graph is therefore fallacious. There are several minor blemishes; for example, a Lancashire firm cannot properly be called a Midland firm. Descriptions of examples of outbreaks are exceedingly well done; the numerous photographs are good and in themselves instructive; opinion is sound and well balanced. There is no better book than this on food control, and the few errors but enhance by contrast the general high standard of writing and production. But, example being more efficacious than precept, I can best commend this book by obtaining a copy for myself—and this I have done.

C. METCALFE BROWN.

BRITISH MEDICAL JOURNAL
LONDON
SATURDAY JANUARY 9 1954

CEREBRAL ARTERIOGRAPHY

Moniz, by performing the first successful carotid arteriogram in 1927, made possible the accurate diagnosis and surgical treatment of certain of the cerebral vascular disorders. His discovery also provided a new method of localizing, and in some cases of identifying, intracranial expanding lesions and a means of studying the cerebral circulation. After careful animal experiments he and his colleague Lima used a 70% solution of strontium bromide as contrast medium, radiographs being exposed as it passed through the cerebral vessels. This substance was soon found to be unsuitable, but with a 25% solution of sodium iodide satisfactory arteriograms were obtained, the medium being injected into the exposed common carotid artery. Sodium iodide was used until 1931, by which time over three hundred arteriograms had been performed and a considerable experience of the normal and abnormal cerebral vascular tree obtained. A 25% colloidal suspension of thorium dioxide (thorotrast) was then substituted as contrast medium, and it proved to be safer than sodium iodide although theoretically dangerous in view of its radioactivity and retention in the liver.

An important development was the introduction of percutaneous puncture of the carotid artery. But this method was of limited use with thorotrast as the contrast medium, for it is irritant if injected outside the vessel. Diodone was first used by Gross in 1939, but its use did not become extensive until Engeset perfected the percutaneous method of injection in 1944. The radiological and operative technique was further developed by Lindgren, and cerebral arteriography is now established as a routine procedure, practised and accepted in all neurological centres. Moniz in 1933 had also started performing vertebral arteriograms in order to demonstrate vessels of the posterior fossa and the posterior cerebral arteries. Four methods of vertebral arteriography are now in use. The percutaneous methods include puncture of the artery in its canal in the cervical spine, and puncture between the arch of the atlas and the occipital bone. The open methods entail exposure of the vessel close to its origin from the subclavian artery or the passage of a catheter up the radial artery.

The indications and scope of cerebral arteriography were fully described by Bull in 1949.[1] Its greatest value is in demonstrating the source of subarachnoid or intracerebral haemorrhage. Congenital aneurysms of the cerebral vessels are the commonest cause of subarachnoid haemorrhage, and cerebral arteriography has made possible the surgical treatment of these lesions, which offers good prospects of cure.[2] Early cerebral arteriography is therefore indicated so that the aneurysm may be identified and treatment started. The examination, if performed soon after a haemorrhage, does not seem to increase the risk of further bleeding. Multiple radiographic projections may be necessary to demonstrate the smaller aneurysms, and if bilateral carotid arteriography fails to show an aneurysm vertebral arteriography should follow. Cerebral angiomata (arteriovenous malformations) may present with subarachnoid haemorrhage, epilepsy, hemiparesis, or headache, and many can be removed. Mackenzie, analysing the clinical findings in 50 proved cases of cerebral angioma, found haemorrhage to be the presenting incident in 15.[3] Intracerebral haematomata, whether or not associated with aneurysms or arteriovenous malformations, may respond to treatment by evacuation, and arteriography will often show their position.

The localization of cerebral tumours depends on their proximity to the large cerebral vessels, whose displacement and distortion may be identified, or on the demonstration of pathological vessels, whose character will often suggest the nature of the lesion. In particular an exact diagnosis may often be made of meningioma, malignant glioma, or metastases. It was at one time thought that the deep tumours of the cerebral hemisphere could be localized only if abnormal vessels were shown, but now that the normal radiological anatomy of the deep veins is well recognized their displacement may indicate the site of a tumour.[4] Carotid arteriography is indicated only if the side in which the expanding lesion lies is clear clinically or from skull radiographs. If the side cannot be determined, pneumography is the examination of choice, but has the disadvantage over arteriography that surgery is more likely to be required immediately. Vertebral arteriography is indicated only for vascular lesions of the basilar system and for expanding lesions in the distribution of the posterior cerebral artery. With the exception of haemangioblastomata, particularly when they are multiple, it is of limited value for the localization of

[1] *Proc. roy. Soc. Med.*, 1949, **42**, 880.
[2] Norlén, G., and Olivecrona, H., *J. Neurosurg.*, 1953, **10**, 404.
[3] *Brain*, 1953, **76**, 184.
[4] Krayenbühl, H., and Richter, Hs. R., *Die Zerebrale Angiographie*. Stuttgart: Georg Thieme Verlag. 1952.
[5] Broman, T., and Olsson, O., *Acta radiol. (Stockh.)*, 1948, **30**, 326, and 1949, **31**, 321.
[6] Lin, P., *et al.*, *J. Neurosurg.*, 1953, **10**, 367.

posterior fossa tumours, and ventriculography is nearly always the method of choice.

Complications of the procedure result from errors of technique or from the effect of the contrast medium on the cerebral vessels. Errors of technique may cause cerebral embolism or the formation of a haematoma at the puncture site. Diodone has been shown by Broman and Olsson to alter the blood–brain barrier, and this effect varies directly with the strength of the solution and the time of application.[5] It is this effect on the blood–brain barrier (or vascular spasm, which probably causes the transient hemipareses) which may complicate arteriography. This complication is more frequent in patients with severe cerebral arteriosclerosis or hypertension, and the examination may be contraindicated for them. Patients with large tumours and high intracranial pressure occasionally become unconscious after arteriography. This is probably due to oedema of the tumour and surrounding brain causing a tentorial pressure cone. In these cases arteriography may be as dangerous as ventriculography. Where clinical and radiological evidence suggests the presence of a large benign tumour, such as a meningioma, arteriography should be performed only when there are facilities for immediate craniotomy if it should be necessary.

The fact that the contrast medium is responsible for most complications points to the need for continuous search for a non-toxic water-soluble substance. "Urokon" sodium 30% (an organic iodine compound) has been claimed to be safer than diodone and is less disturbing subjectively, but in 1 of 100 patients Chamberlain reported complications.[6] Recent advances in radiographic technique include simultaneous radiography in two planes; this facilitates examination with a smaller volume of contrast medium. Rapid serial radiography has proved to be of value in the study of the normal and abnormal cerebral circulation and in the demonstration of pathological vessels.

Cerebral arteriography has now a secure place in the diagnosis of neurological diseases, particularly the vascular disorders. It has to some extent replaced pneumography in the localization of intracranial expanding lesions, but these examinations are nevertheless complementary, the choice depending on the nature of the suspected lesion and personal preference of the clinician or radiologist. With the advance of radiographic techniques, it can be confidently predicted that the finer details of the cerebral blood vessels will be demonstrated in the living, for at present only relatively large vessels and lesions can be shown.

CORONARY DISEASE AND WORK

Since the publication of the Registrar-General's analysis[1] of occupational mortality for the years 1930–2 it has been known that mortality from coronary heart disease is considerably higher among the professional classes than among unskilled workers. This observation is all the more striking because experience of most other diseases, including most other forms of heart disease, suggests that where incidence is related to social and economic circumstances it is usually highest in the poorest classes. The striking exception of coronary disease has inevitably provoked discussion of aetiology; and emotional stress,[2 3] diet,[1] and the sedentary nature of work[4] have all been suggested as contributing agents.

In a recent report[5] Dr. J. N. Morris and his colleagues have added the useful observation that there are differences in the experience of coronary disease between workers in occupations usually regarded as belonging to the same social class. They have examined sickness and mortality records of drivers, conductors, and guards aged 35–64 employed by the London Transport, and, interpreting the first absence from work because of coronary heart disease as the first clinical episode, they have shown that about one-fifth of the cases first present as angina pectoris, about half as coronary thrombosis which is not rapidly fatal, and between one-quarter and one-third as coronary thrombosis which results in death within three days. After a detailed comparison of the morbidity and mortality experience of conductors with that of drivers, they conclude that conductors have less coronary disease, and that their disease appears at a later age and follows a more benign course. In discussing these results Morris and his colleagues consider, as it seems right to do, the possibility of both constitutional and environmental differences between persons in the two occupations. They are particularly attracted, however, by the possibility that lack of physical activity is a contributing factor in aetiology, a suggestion made by Stocks[4] and supported by a comparison of the mortality experience of clerical workers and mineworkers.[6] Morris and his colleagues have examined this possibility more closely, and have assembled an impressive body of evidence consistent with the view that mortality from coronary heart disease is inversely related to the amount of physical effort which the occupa-

[1] Registrar-General for England and Wales. *Decennial Supplement* 1931, *Part IIA, Occupational Mortality*. London. 1938.
[2] Ryle, J. A., and Russell, W. T., *Brit. Heart J.*, 1949, **11**, 370.
[3] Stewart, I. McD. G., *Lancet*, 1950, **2**, 867.
[4] Stocks, P., ibid., 1951, **1**, 351.
[5] Morris, J. N., *et al.*, ibid., 1953, **2**, 1053 and 1111.
[6] Logan, W. P. D., ibid., 1952 **1**, 758.
[7] Morris, J. N., *et al.*, *British Medical Journal*, 1952, **1**, 503.

tion requires. It is clear that physical activity is not the only important factor in the aetiology of coronary heart disease; it cannot, for example, explain the higher incidence in general practitioners than in consultants.[7] There is indeed every reason to suppose that, as in most other diseases, both genetic and environmental agents are at work, and it is most unlikely that the environmental component can be attributed to a single agent. Nevertheless the relationship between physical activity and experience of coronary disease seems firmly established, and any acceptable discussion of aetiology must take account of it.

These findings in coronary heart disease, like some others related to the aetiology of common diseases, raise an important issue. The environmental changes which have contributed so much to the decline of mortality since the early years of the nineteenth century were brought about by public authorities, and depended for their effectiveness hardly at all upon the co-operation of the individual. But many of the aetiological agents now under consideration are of quite a different character: what to eat, whether to smoke, and how much to exercise are intensely personal questions which cannot be decided solely by Acts of Parliament, and responsibility for answering them must inevitably rest to a large extent with the individual. At present the task of establishing the significance of food, smoking, and exercise in aetiology is sufficiently exacting, and the investigator should not be deterred by the practical implications of positive findings. But it is as well to recognize that when positive findings are forthcoming they suggest no easy remedy, but on the contrary raise issues, personal as well as public, for which the experience of nineteenth-century public health has hardly prepared us.

HEART DISEASE AND PREGNANCY

The management of the pregnant woman with heart disease calls for a high standard of judgment, skill, and watchfulness on the part of the attendants. The close co-operation which should obtain between obstetricians and physicians is exemplified by a joint report at p. 70 of this issue of the *Journal* on 250 pregnancies in 175 women with rheumatic heart disease seen at the National Maternity Hospital, Dublin, during the four years 1948–51. The authors say that these cases are drawn from a population which does not practise contraception, therapeutic abortion, or sterilization, and they argue that a true picture of the natural course of rheumatic heart disease in relation to pregnancy is obtained. The follow-up of the cases was unfortunately limited to a maximum of four years, but many valuable lessons are to be learnt, or rather learnt afresh, from this review.

The assessment of the probable risk of pregnancy in these women is best based, as Professor Bramwell pointed out in this *Journal* last year,[1] on the woman's exercise tolerance before pregnancy, but often the patient is not seen until the cardiac efficiency is already influenced by the pregnancy. The previous obstetric history, age, social surroundings, and personal temperament and wishes of the patient have all to be taken into account in giving guidance and hazarding a prognosis. But the immediate prognosis is governed above all by the quality of antenatal care, and MacRae's[2] recent description of the details of careful attention which enabled him to report 228 consecutive cases without maternal death in pregnancy or labour is worthy of close study. The heart condition can be expected to deteriorate with increasing parity, probably because of the coincident increasing age; but the severer degrees of disability occur disproportionately often in younger women, probably because of the greater chance in them of recrudescence of acute rheumatism. Auricular fibrillation, respiratory infection, and anaemia are important factors in precipitating heart failure during pregnancy. The maximum strain on the heart is between the 28th and 36th weeks; it might be profitable therefore to admit these women to hospital for rest at this time rather than for the customary two or three weeks before term. Only exceptionally does cardiac failure begin in the last month of pregnancy, and the induction of premature labour during that time is therefore irrational. In cases of mitral stenosis, valvotomy during pregnancy is likely to be increasingly performed, for in some of them it will avert the need to consider therapeutic abortion; the operation may also be preferred when severer degrees of disability show little improvement with medical treatment, or when acute pulmonary oedema has occurred or is threatened. In the management of labour the salient points are the avoidance of caesarean section except for purely obstetric indications, the use of morphine and pethidine for analgesia, supplemented later if necessary by gas and air or gas and oxygen, the shortening of the second stage by the judicious use of forceps under local analgesia, and the avoidance of post-partum haemorrhage. The lying-in period should be extended to at least three weeks, and the woman should then be referred to a heart clinic for further help and supervision, for the obstetrician is dealing with merely one episode in her life.

In the Dublin series, 11 of the 175 women died during the short time of follow-up, 5 of them more than one year after confinement. The conclusion is drawn that these five deaths were not related to pregnancy, but it seems likely that the extra burden, not of the pregnancy itself but of looking after another baby, especially in poor surroundings, materially shortened the mother's life. Of the 6 women who died during pregnancy or within one year of delivery 5 were under 30 years of age, and all were unbooked patients who were admitted as emergency cases and in poor condition. It is discouraging to read that in some cases seen neither the patient nor her doctor was aware that heart disease

[1] Bramwell, C., *British Medical Journal*, 1953, **1**, 897.
[2] MacRae, D. J., *J. Obstet. Gynaec. Brit. Emp.*, 1953, **60** 650.

existed until complications ensued. Heart disease has become one of the commonest causes of maternal mortality, and early diagnosis and scrupulous antenatal care are imperative if fatalities are to be avoided.

MEASUREMENT OF SICKNESS

While the collection of mortality statistics could hardly be made more complete in Britain except in small particulars, the collection of morbidity statistics, other than those of notifiable infectious diseases, is slight in comparison. Malignant disease was early singled out for special study of morbidity, at first by the Radium Commission in 1930, and in recent years the net has been cast increasingly widely by the General Register Office.[1] A few weeks ago a useful study of general practitioners' records by Logan[2] was discussed in these columns,[3] and now a further contribution to this difficult field of inquiry comes from the General Register Office.[4] It gives information, first, on general morbidity obtained by the Survey of Sickness, secondly on admissions to and discharges from mental hospitals, and thirdly on cancer registration. The last section includes a table showing for twenty-one cancer sites and fourteen regions of England and Wales an analysis of the time intervals from the earliest symptom or sign of cancer to the date of registration or treatment. While no very precise significance can be attributed to these intervals for reasons given by the Registrar-General, they may prove to be of particular interest for comparison with figures obtained in subsequent years (these refer to 1947–8), but even these may provoke thought. For instance, by means of some simple calculations a comparison may be made for the different geographical areas between the proportion of cases with intervals of less than 24 months and the proportion with intervals of 24 months and over. For all the centres and hospitals 16.5% of the cases had intervals of 24 months and over. In the metropolitan area 15% had intervals of 24 months and over, and there was no difference between the teaching and non-teaching hospitals there. Newcastle and Liverpool also had 15%, and Leeds and Birmingham 16%. Sheffield, East Anglia, Oxford, and the South-west followed with 18%, and Manchester with 19%. Finally came Wales with 28%. The number of cases is rather small in Wales and its relative position should be accepted with reserve, but the figures do suggest the need for some special inquiry there if only to ascertain their significance more clearly. Similar comparisons may be made of these intervals between the different cancer sites, but they must at present be even more hazardous if only because of the different rates at which cancers can grow at different sites.

The figures for the mentally sick refer only to those treated in Health Service hospitals; the numbers treated in private institutions, psychiatric clinics, and prisons are unknown. At the end of 1949 there were in mental hospitals 3.4 per 1,000 civilian population, and 68% of direct admissions were first admissions. The rate of admissions increases as age advances: for men aged 65 and over the rate was 673 per 100,000 population in the age group, compared with 300 for all men, and for women aged 65 and over it was 968, compared with 368 for all women. Like the cancer statistics those for mental illness will gain in significance as the years pass and more figures become available for comparison. This volume is the first on morbidity statistics to be added to the Registrar-General's annual review. It is a break with a 125-years-old tradition that is both welcome and worth repeating.

[1] Stocks, P., *Cancer Registration in England and Wales*, Studies on Medical and Population Subjects, No. 3. H.M.S.O. 1950.
[2] *General Practitioners' Records*, Studies on Medical and Population Subjects, No. 7. H.M.S.O. 1953.
[3] *British Medical Journal*, 1953, **2**, 1038.
[4] *Registrar-General's Statistical Review of England and Wales for year 1949: Supplement on General Morbidity, Cancer and Mental Health.* H.M.S.O. 7s. 6d.

EXCHANGE OF PRACTICES

During the last four years the Medical Practices Advisory Bureau of the B.M.A. has made over 2,000 introductions with a view to exchange of practices, but fewer than 20 doctors have been able to conclude satisfactory arrangements. It is not difficult to find reasons for this discouraging result. A recent survey by the Bureau suggests that the majority are wanting the same thing—a more desirable area without too great a drop in income. Certainly the inducement of a bigger income is insufficient to attract doctors to industrial areas. Many will only consider an exchange if certain limiting conditions are fulfilled, and are apparently prepared to wait indefinitely in the hope of finding just what they need. At the end of last October, according to the survey, there were at least 70 doctors anxious to exchange practices. Experience shows that many of the secondary difficulties which must inevitably accompany negotiations, such as exchange of houses, the presence or lack of social amenities or of educational facilities, are not insuperable.

The preliminary steps towards exchange are necessarily confidential, and in order to give publicity to the opportunities which are available, together with details sufficient to invite inquiry, while concealing any information by which the doctor or practice could be identified, we publish in the advertisement columns of this issue (p. 24) a list comprising 70 practices offered for exchange. Introductions and advice on procedure can be obtained by application to the Medical Director of the Medical Practices Advisory Bureau. It is impossible to say whether regular publication of a comprehensive list of practices for exchange will increase the exchanges effected, but this tentative experiment of advertising a large number together will at least give a clearer picture of the possibilities of the scheme and of the available facilities.

A TREATMENT FOR ECZEMA

In making therapeutic trials investigators have often had difficulty in discounting the human factor. If the new treatment gives apparent initial success the enthusiasm of the physician is apt to give rise to the over-optimistic reports which are all too familiar and which have in many cases hampered the progress of medicine, caused much waste of time and money, and added false hopes and disappointment to the patient's burden. Thus it is that exaggerated claims for new remedies are prolific, and the disillusioning process lags too far behind. The investigation conducted by Dr. J. H. S. Pettit into

linoleic and linolenic acids in the treatment of eczema (page 79) is a happy exception. Since the first reports of this treatment—most of them, as Dr. Pettit points out, conducted without controls—the treatment has been recommended in advertisements and elsewhere for various types of eczema and for a variety of other dermatoses. As a result these preparations have no doubt been used extensively both in general practice and in hospital. A glance at Dr. Pettit's tables will illustrate the variable course of eczema under different treatments, and it is easy to see how a wrong judgment can be formed if only a few cases are treated. To add to the illusion most doctors, quite naturally, tend to remember with joy the one or two apparent cures and to forget the half-dozen cases in which nothing happened.

Clinical experience grows slowly, and it may be that further experience will eventually attach a somewhat greater value to these fatty acids than this report suggests. But it is probable that the general consensus of dermatological opinion has, by a slow accumulation of clinical impressions and by more limited trials, already reached substantially the same conclusions for which Dr. Pettit now provides statistical support. Indeed, this probably applies not only to atopic eczema but to the various other dermatoses for which this type of treatment has been enthusiastically recommended.

CHLORPROMAZINE FOR HYPOTHERMIA

In a recent annotation[1] entitled "A New Drug" we observed that clinical findings were published before the results of a pharmacological investigation of the drug in question ("4560 R.P.," now known as chlorpromazine or "largactil"), and mentioned the need for research on some aspects of the drug's action. In commenting thus we failed to do justice to the work of Courvoisier and her colleagues[2] at the Rhône-Poulenc laboratories. Their paper was published in January, 1953, after the appearance of the report by Laborit, Huguenard, and Aulluaume,[3] to which we have already referred.[1] Courvoisier's work showed, among other things, that chlorpromazine inhibited the effect of vagal stimulation but did not appreciably diminish the action of acetylcholine. For this reason chlorpromazine was described as a ganglion-blocking agent, although no evidence was given of any action on sympathetic ganglia. Much prominence has been given to this feature of its action, and a ganglion-blocking effect has been held to explain the fall of body temperature which it causes. Both Dundee and his colleagues[4] and Smith and Fairer[5] in their recent papers on hypothermia in this *Journal* appear to subscribe to this view. It is, of course, true that the sympathetic fibres to the skin cause vasoconstriction in response to cold, but it has long been known that the most important organs concerned in heat production are the skeletal muscles. Their innervation is not through the autonomic system, but through the voluntary system, and therefore the suppression of shivering by curare or other substances such as chlorpromazine has nothing to do with autonomic or ganglion blockade.

As to the question of how chlorpromazine, or a mixture of it with pethidine and promethazine, causes a fall of body temperature, one possibility is that it exerts a central action and abolishes the reflex impulses to the skeletal muscles in the same way as does any form of deep anaesthesia. There is also the possibility that it acts directly on the muscles themselves, depressing their metabolism. Evidence against this second view is given by Peruzzo and Forni,[6] who have determined the effect of chlorpromazine on the oxygen consumption of tissue slices from liver, kidney, and brain. They found that the oxygen consumption of slices of the cerebral cortex of the rat was greatly diminished, but that that of slices of liver and kidney was unaffected. These results strongly suggest that the effect of chlorpromazine is central.

There is, however, nothing new in the finding that substances of this kind will reduce body temperature. Quinine has perhaps the oldest claim to this action, and more recently[7] it has been shown that pethidine, procaine, diphenhydramine, and quinidine have it too. In our correspondence columns last week (p. 42) Dr. C. Langton Hewer gave some timely advice to anaesthetists who are thinking of using chlorpromazine. Until careful quantitative comparisons in further animal experiments have established that chlorpromazine is definitely superior to other drugs, it would seem wise to use more familiar tools, such as pethidine, in the trial of methods of anaesthesia devised to make surgery safer for the poor-risk patient.

1 *British Medical Journal*, 1953, **2**, 1149.
2 *Arch. int. pharmacodyn.*, 1953, **92**, 305.
3 *Presse méd.*, 1952, **60**, 206.
4 *British Medical Journal*, 1953, **2**, 1237, 1244.
5 Ibid., 1953, **2**, 1247.
6 *Presse méd.*, 1953, **61**, 1463.
7 Dutta, *Brit. J. Pharmacol.*, 1948, **3**, 246.

HOSPITALS AND THE PUBLIC

About a year ago a report of the Central Health Services Council entitled "The Reception and Welfare of In-patients in Hospitals" was sent out to hospital management committees. Commenting on this we remarked that "lack of information probably causes patients and their relatives more worry than anything else," and we mentioned some of the ways by which the bewilderment and apprehensiveness of the ordinary patient could be relieved.[1] The Portsmouth Group Hospital Management Committee has recently adopted a series of recommendations put forward by the secretary of the group with a view to improving relationships with the public. One of the dangers of a nationalized service is that hospitals should come to be impersonally regarded as a special type of workshop, with problems little different from those of an industrial concern. The burden of the Portsmouth report is that a hospital must exert itself to keep the good will of the public, and that efforts made in this direction will be well

1 *British Medical Journal*, 1953, **1**, 264.
2 Ibid., 1953, **2**, 683.

repaid. In particular there is still room for much improvement in the reception of patients and their relatives. Out-patient departments should be brightened, and when patients have to be kept waiting for a long time someone in authority—perhaps the sister in charge of the department—should give them a full explanation of the reason for delay. All complaints, even the unjustified ones, should be sympathetically listened to and answered, so that no patient or relative has any reason to retain a sense of grievance. At Portsmouth they rightly attach great importance to the handling of telephone calls: well-trained, efficient, and helpful telephone operators can do much for the reputation of a hospital.

It has been estimated that in the Portsmouth area one person in every eight comes into some contact with local hospitals every year, and the management committee is one of the largest employers in the neighbourhood. Thus the hospital touches the lives of a large proportion of the population. Where an active "league of friends" has developed round a particular hospital so has the association of the hospital with the neighbouring community become more firmly established. It is good to learn that the Portsmouth Group Hospital Management Committee has agreed that "if the hospitals are to provide the best service, the closest co-operation and confidence of the family doctor must be enlisted." The Hadfield report[2] has given emphasis to the valuable suggestion that local doctors might be asked for their views on some of the difficulties which arise in the relationship between hospitals and general practitioners. Portsmouth is not the only hospital group to take action on the Central Health Services Council report, but there is still much to be done before the common complaint, "They never tell me anything," is no longer heard.

FLEXIBLE ENDOSCOPES

An idea that may revolutionize the design of endoscopes was last week the subject of a communication from H. H. Hopkins and N. S. Kafany,[1] of the Imperial College of Science and Technology, London. They describe how light may be transmitted through a bundle of glass fibres even when the bundle is curved quite sharply through an angle of 90 degrees. The simplicity of this system of transmitting light images, over that of the existing gastroscopes for instance, which have up to 50 lenses, may add great reduction in manufacturing costs to increased flexibility in performance. With a bundle 4 in. (10 cm.) long made by these workers a bending radius of less than 2 in. (5 cm.) was achieved "without any deterioration in the image quality," and the theoretically expected resolving power of 100 lines to the inch (40 to the cm.) with the fibres used is reported to have been easily obtained. Similar experiments in Holland carried out by A. C. S. van Heel are reported in the same issue. He was led to them by a consideration of the eye structure of some insects.

[1] *Nature* (*Lond.*), 1954, 173, 39.

THE NEW YEAR HONOURS

The list of New Year Honours (see p. 95) contains, as is usual, the names of medical men and women who have achieved eminence in their profession at home, in the Services, and in many Commonwealth and Colonial countries. At the top of the list comes Lord Webb-Johnson, who is promoted to Knight Grand Cross of the Royal Victorian Order. Among the new medical knights comes Professor E. C. Dodds, F.R.S., director of the Courtauld Institute of Biochemistry at the Middlesex Hospital. He was appointed professor of biochemistry in the University of London in 1925 while still in his twenties. Professor Dodds is known all over the medical world for his investigation of the chemical and physiological properties of internal secretions, and for work which led, about fifteen years ago, to the synthesis of stilboestrol. His colleagues, here and elsewhere, will be delighted that the Queen has been pleased to honour him. The dental as well as the medical profession will be gratified by the knighthood awarded to Mr. E. W. Fish, chairman of the Dental Board of the United Kingdom. Mr. Fish, who has been dental surgeon to St. Mary's Hospital and the Royal Dental Hospital, has a distinguished record as a teacher and as an investigator of dental and oral disease. In 1952 he was president of the eleventh International Dental Congress in London. The honour of knighthood has also been awarded to Dr. F. T. Rees, who has recently retired from the post of Director-General of Medical Services, Ministry of Pensions (which is now merged with the Ministry of National Insurance). Dr. Rees joined the staff of the Ministry in 1919, and thus was closely concerned with the pensions work which followed the two great wars. Australia will soon be much in the news, and it is fitting that two Australian medical men complete the list of new knights. Dr. B. H. Swift, gynaecological and obstetric surgeon in Adelaide, has many friends in this country. A graduate of Cambridge University, he is a Fellow of the Royal College of Obstetricians and Gynaecologists, and vice-chairman of the Australian Council of the College. A few years ago he was president of the South Australian Branch of the B.M.A. Dr. H. W. Wunderly, who was elected F.R.C.P. last year, is a specialist in diseases of the lungs. Before his appointment in 1947 as Director of Tuberculosis in the Department of Health at Canberra he was a physician in Adelaide.

Some well-known names are in the list of those awarded the C.B.E., but there will be particular pleasure that a medical woman in Australia, Dr. Kate I. Campbell, is thus honoured: she is a paediatrician in Melbourne. Dr. G. A. Clark, Principal Medical Officer at the Ministry of Health, and formerly dean of the faculty of medicine and professor of physiology at Sheffield University, receives the C.B.; and Dr. H. W. Mulligan, director, West African Institute for Trypanosomiasis Research, and Dr. W. G. Wickremesinghe, who has been Acting Director of Ceylon's Health Services, receive the C.M.G.

CLINICAL PATHOLOGY IN GENERAL PRACTICE

INVESTIGATION OF OUTBREAKS OF INFECTION

BY

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No short article can adequately cover the whole of the investigation of epidemics of communicable disease, so a number of restrictions have to be introduced. I shall deal only with diseases that occur in Britain, and largely with diseases for which the laboratory can, in the present state of knowledge, give practical help. Moreover, since it is with the investigation of localized outbreaks of communicable disease rather than with widespread epidemics that the general practitioner is likely to be concerned, the discussion is similarly restricted.

It is convenient to recognize three sorts of outbreak: one in which a number of cases occur as nearly as may be simultaneously; one in which infection appears to be spreading through the community; and one in which the so-called "dropping" cases of a disease occur at intervals. None of these histories is pathognomonic of any particular method of spread, but the explosive outbreak is often due to massive contamination of a common foodstuff, and the dropping-case type of outbreak is commonly due to a chronic carrier of the infective microbe. These two sorts of outbreak are also those in which the general practitioner may be in the best position to assist—the explosive outbreak because he is the first on the spot and therefore best placed to secure material for laboratory investigation; the dropping-case outbreak because he alone may be in a position to recognize its occurrence and envisage the common contacts of the patients.

In the investigation of a suspected outbreak of infection there are several steps. The first is the establishment of a precise diagnosis in the suspected cases, and the second is the taking of a careful history of the patients and of the outbreak. In some cases these two steps—diagnosis and history taking—indicate so closely the source of infection that for practical purposes further investigation is superfluous. More often, however, the third step is an attempt to trace the source from which the latest batch of patients became infected. At the same time an attempt is made to discover other victims of the infection who have as yet shown no signs of disease; sometimes it is also possible to determine the susceptibility of contacts to the disease. Lastly, it may be necessary to try to find out how the infection was spread—by direct contact or by indirect methods such as food, drink, air, or fomites.

Diagnosis and History

An accurate diagnosis and an accurate history for the individual patients are the first requirements. In many cases the "diagnosis" may be the name of a well-recognized disease. In others, however, it may be a syndrome, observed to occur in epidemic fashion, but not yet widely recognized. In the latter group accurate definition of the syndrome is most important.

The history needs to include the dates of onset of the disease in each individual patient; details of his activities at the times when, judged from the ordinary incubation period of the disease, he must have been infected; and details of his activities immediately before he fell ill, when he was probably already infective.

In addition to the history of the illness in individuals, we need to construct a history of the incident as a whole, and this has to take account of the persons who were not ill as well as those who were. It is important, especially in outbreaks that may be food-borne, to assess the number of persons exposed to infection, and in all kinds of epidemic a comparison of the attack rates in various groups of the population—different classes in a school, different ages, the two sexes, the various wards in a hospital—may often give a strong lead to the subsequent bacteriological investigations.

In some instances diagnosis and history may be all that is possible, for want of methods for cultivating the responsible microbes or other means of laboratory confirmation. Even so, it may be possible to infer the way in which the disease is spread and methods for its prevention.

However, there are numerous occasions when laboratory help is indispensable to the proper investigation and control of the epidemic. Laboratory help comes first in helping to establish the diagnosis of the disease, and at this stage it has two functions. The first is to put a precise name to the patient's illness—to convert the label of "P.U.O." to the diagnosis of typhoid fever, to distinguish the streptococcal from the non-streptococcal sore throat, to recognize the true virus influenza among the host of "'flus." These distinctions can often, with experience, be made on clinical grounds alone, especially in the face of a general epidemic, but the laboratory should be able to make the distinction with more certainty and in the atypical cases. For this to be most useful the laboratory must be prepared to issue, and the practitioner to accept, preliminary reports which may be subject to some revision when the tests are complete.

The second function of the laboratory is the "type identification" of the infecting organism. In many cases the members of a species of pathogenic bacteria or viruses can be classified into a number of types which are stable under natural conditions. Then, if two patients are found to be infected with one species of microbe but of two different types, we can conclude that they became infected from different sources and are not part of one epidemic. If both are infected with one type they may well have acquired the infection from a common source, but the

TABLE I.—*Microbes that Cause Epidemics and Can be Classified Into Types*

Microbe	Disease	Typing Method Employed on Microbe
Salmonella typhi	Enteric fever	Bacteriophage
" *paratyphi*	" "	"
Other *Salmonella* species ..	Food-poisoning	Serology
Escherichia (*Bacterium*) *coli* ..	Some gastro-enteritis in infants	"
Shigella species	Dysentery	"
Streptococcus pyogenes (Lancefield's group A haemolytic streptococci)	Scarlet fever, sore throat, puerperal sepsis, etc.	"
Staphylococcus aureus	Food-poisoning, sepsis, etc.	Bacteriophage
Streptococcus pneumoniae (pneumococcus)	Lobar pneumonia	Serology
Corynebacterium diphtheriae ..	Diphtheria	Morphology in culture, serology, and physiology
Influenza virus	Epidemic influenza	Serology

degree of certainty that can be put on this conclusion depends on the frequency with which the various types occur in the population.

Of the microbes that cause epidemics, those for which type identification is possible are listed in Table I, but a warning may be added here. The techniques of type identification are commonly difficult and the materials needed are usually available in only a few specialized laboratories. This means that there may be a few days' delay before the results of the tests can be given to the practitioner or medical officer of health. It also means that requests for type identification ought to be restricted to investigations where enough material has been collected to make the results useful.

Search for Source of Infection

The diagnosis and the history should indicate what sort of outbreak is occurring, and what investigations are needed to trace its source, to prevent further cases in the immediate future, and to prevent the occurrence of further outbreaks.

In outbreaks apparently due to infection of a common foodstuff an attempt is first made to demonstrate bacterial contamination of the food remnants, and then a search is made for carriers among the persons who had handled the food. In outbreaks consisting in dropping cases of bacterial infection a search may be made for chronic carriers among contacts and perhaps also for intermittent contamination of food. When there is evidence that a disease is spreading from case to case through a community we are concerned to discover those remaining susceptible to infection and also the potential dispersers of infection; in some examples of this type it may be possible to control the outbreak by isolating all infected persons, but often specific protection of the remaining susceptible persons may offer more hope of success.

Laboratory assistance in the investigation of the source of outbreaks is thus most often required in a search for healthy carriers and for other animate or inanimate sources of the causal organism.

Truly chronic healthy carriers are particularly important in the propagation of typhoid fever, and they also play a part in the spread of streptococcal and staphylococcal infections. In food-poisoning due to salmonellae, and in dysentery, chronic carriers are unimportant, but patients recovering from the disease may continue to excrete the organisms and infect others.

In attempting to pin responsibility for an epidemic on a carrier discovered during investigations made after cases have occurred, it may be difficult to be certain that the carrier was not really a victim rather than the cause of the outbreak, but in either case he may still be a cause of further spread if opportunities occur.

In surveys for possible dangerous carriers it is most important, though often difficult, to examine everyone who may have been concerned. The kitchen staff may include a number of part-time members who are often understandably reluctant to submit to examination; repeated inquiry may be needed to establish the full complement.

The specimens to be obtained from suspected carriers in investigations of some of the more important infections are given in Table II. In the enteric fevers especially, the carrier state may sometimes be recognized by finding a raised serum antibody titre (Widal reaction, typhoid Vi antibody titration), but the interpretation of these tests is often confused by antibodies resulting from earlier prophylactic inoculations. A raised titre of typhoid Vi antibody, however, is found only in persons who are still carrying the living organisms.

TABLE II.—*Specimens Required from Suspected Carriers*

Disease	Specimens
Enteric fever	Faeces and urine Serum for detection of raised antibody titre in chronic carriers or convalescents
Salmonella food-poisoning Dysentery Staphylococcal infections and food-poisoning	Faeces Swabs from nose and throat, from skin of hands, and from any active or healing septic lesion
Streptococcal infections	Swabs from nose and throat and any septic lesion
Diphtheria	Swabs from nose and throat (or wound)

A raised antibody titre to the streptococcal toxin, streptolysin O, would similarly indicate recent infection with haemolytic streptococci, but this test is not widely used in a search for streptococcal carriers, partly because elevation of the titre is not invariable even with severe streptococcal infections, and partly because streptococcal infections are so common that only a method giving retrospective type-specific diagnosis would be useful. No such test has yet reached the stage of practical application. Other diseases in which antibody titration may be helpful include influenza, psittacosis, Q fever, undulant fever, and Weil's disease.

Relative Dangers of Carriers

With the intestinal infections, all carriers are commonly regarded as potentially dangerous. On the other hand, healthy persons who yield only small numbers of haemolytic streptococci, even of the pathogenic group A, are of little danger to their fellows, and there is good evidence that heavy nasal carriers are the persons particularly apt to spread the infection.

The hope animating any search for carriers among the contacts of the patients in an outbreak is that we may find a single person infected with the microbe causing the outbreak, and that he or she had the opportunity to spread the disease. Sometimes this hope is realized, and removal or neutralization of the carrier may, provided all the victims are accounted for and prevented from further dispersal, end the epidemic. Often, however, several carriers are found; one of these may perhaps be the source and the others victims—a distinction that may sometimes be possible from the history of the outbreak.

The presence of numerous carriers may also indicate that the microbe has already spread widely through the population, and may indeed have already infected many or all of those susceptible. In some circumstances this may indicate that the epidemic is burning itself out; in others, such as a hospital ward, it may show that the only ways of preventing further infection are by specific protection of the remaining susceptible patients or by closing the pathways along which infection is transmitted, including the isolation of infected persons.

Specific protection may be by the use of general chemoprophylaxis or, in diphtheria and smallpox particularly, by immunization. With diphtheria, indeed, it is also possible to distinguish the susceptible persons from the immune persons by means of the Schick test.

Animal Reservoirs

In considering the source of some epidemics, animals have to be considered. The *Salmonella* organisms responsible for food-poisoning may be pathogens or harmless commensals of domestic animals—the risk from infected duck eggs is so well known now that an infected patient who has had a duck egg within the past few days is often hardly questioned further. Epidemics of psittacosis arise from contact with sick birds, not only parrots; epidemics of bovine tuberculosis and Q fever start with infection derived from cattle or, in the latter case, other animals; and infection in Weil's disease is derived from rats.

Method of Spread of Infection

Inseparable from the investigation of the source of the epidemic—using "source" for the person or animal in whom the microbe was previously living—is the investigation of the way in which the organism was spread. We can distinguish spread by food and drink, by direct or indirect contact, by the air, and by insect vectors. With the possible exception of flies, spread by insects is so rare in this country

that it is not considered here. The distinction between these methods usually has to be made from the history of the outbreak and from comparison of attack rates on different groups of people who had various degrees of association with one another, or were exposed to various possible sources of infection.

Food-borne outbreaks are commonly, though not always, abrupt in onset; accurate history-taking often leads to a clear indication of the source of the infection. The enteric diseases and food-poisoning are always spread by infected or toxic food, and in the investigation of such outbreaks collection of samples of foodstuffs is important; these should be sent to the laboratory immediately, because, if kept, the pathogenic organisms may be overgrown by saprophytes. With diseases like typhoid fever, however, which have an incubation period of 10 days, it is quite likely that contamination of food or water with the typhoid bacillus has ceased by the time that investigations are begun. Some help may still be given by laboratory investigations, which may reveal, for example, faecal contamination of water supplies, faulty food-handling habits, or inadequate heat treatment of milk or ice-cream, and so indicate methods for the prevention of further outbreaks.

In both "dropping-case" and "spreading" outbreaks in hospitals hopes of prevention lie in investigation and the closing of the routes of infection, especially by improvements in the aseptic routine. For this it is often necessary to spend a great deal of time in the affected department, quietly observing the routine as it is followed; it will often be found to differ from that prescribed by authority.

In investigating outbreaks in hospitals and schools it is often possible to obtain evidence of widespread dissemination of the epidemic microbe on bed-clothes, in floor dust, on surfaces, and in the air; and bacteriological investigations of fomites may suggest the route of transmission. It is well to remember, however, that the finding of, for instance, large numbers of streptococci in the floor dust of a school suffering an epidemic of scarlet fever does not necessarily imply that the victims were infected by dust-borne streptococci; it may be that the streptococci in the dust are no more than a by-product of dispersal from carrier to new host by much more direct means.

In one special case the method of transmission of infection may be discovered, but not the person from which the infection is derived. This is the syringe-transmission of infective hepatitis: the causative virus may be carried in the blood of apparently healthy persons and be transferred to others by inadequately sterilized hypodermic syringes or needles; the infecting dose of virus is so small that it may be contained in an almost imperceptible amount of blood.

Conclusion

Clearly, methods for the investigation of all epidemics cannot be prescribed in a short article; all that can be done is to indicate some of the broad lines of approach, and the part that the laboratory can play in the investigations. The medical officer of health, on the epidemiological side, and the laboratory, on the microbiological side, can give guidance to the practitioner on the specimens that should be examined and the investigations that may profitably be made in any particular outbreak. The part played by the Public Health Laboratory Service, which was constituted to give assistance in the investigation of epidemics, was described by Dr. M. T. Parker in a previous article in this series (October 10, 1953, p. 823).

The investigation of outbreaks of infection has often consisted solely in the analysis of numbers of cases and of attack rates on the various sex and age groups of a population that are readily accessible in the, often inadequate, written records. Analyses of attack rates are essential, but to show their real value they have to be done in the first few hours of the investigation, for their first purpose should be to guide the field and laboratory investigations. The source of any but the simplest of epidemics can rarely be found unless the investigations are started as soon as there is reasonable suspicion of the existence of an epidemic, and it will certainly not be found without a concerted clinical and laboratory investigation on the spot. With information gained from such full investigations, retrospective analysis may be expected to indicate the way in which further outbreaks may be prevented.

Next article on Clinical Pathology.—"Examination of Faeces for Infection and Infestation," by Dr. K. B. Rogers.

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MEDICAL AND SOCIAL PROBLEMS OF THE AFRICAN IN INDUSTRY

BY

J. H. JACKSON, M.B., B.S.

The industrial and mining development of the greater part of the African continent is still in its infancy. Full development will result in its attaining a position of great economic and strategic importance in the world, but cannot be carried out without native African labour. The future prosperity of Africa rests upon this, unless some equally suitable type of labour can be found. No true thought or consideration has been given to this fact by those in whose hands the existing development of the continent up to the present has lain. This seems to have been due to ignorance of the economic and social hazards of a policy of *laissez faire*, combined with the fact that labour supply has exceeded demand and the sources have been primitive peoples with a high reproductive rate whose mental horizons and economic needs were until recently of the lowest possible order.

Social Conditions

To-day in a large part of the African continent the industrial and mining development which has taken place has created terrible social conditions associated with poverty, malnutrition, disease, and crime. The terrifying proportions of these social evils appal the mind when viewed in the nakedness of their true facts. The social burden of the corrective measures necessary to deal with the situation now in existence is likely to be extremely heavy if the measures required are to prove effective. Indications are that such measures are beyond the means of the community as at present constituted. The social unrest which must inevitably spring from the continued existence of these conditions is likely to lead to economic and political disaster.

Whether sufficient knowledge or foresight could have been expected from those responsible for the creation of the present conditions one cannot say. Nevertheless I am of the opinion that a repetition of the mistakes elsewhere can be avoided by a knowledge of those of the past. It is the intention of this paper to discuss the medical and social impact of certain procedures which have been adopted to obtain native industrial labour, and the ultimate effect which they are likely to have if imposed upon primitive native peoples. It is based upon five years of general practice in an area where some of the conditions described exist. If it prevents similar conditions arising during the future development of the relatively untouched African territories then its purpose will have been well served.

Migratory Labour

In a large part of Southern Africa a system of migratory labour for the mines, industry, sugar plantations, etc., has been in existence from the outset. It will serve no purpose here to describe and discuss the factors which have resulted in the creation of native reserves where a large proportion of the population is crowded, where the land is eroded and exhausted, and, with present methods of cultivation, incapable of supporting agriculturally the population on it, and where no industries whatsoever exist capable of contributing to the local economy. Suffice it to say that they exist to-day in their stark reality. From these reserves 30 to 40% of the able-bodied males go annually to work elsewhere, leaving their women to till the land. These men depart for a period of six to nine months, sometimes for one to two years, to labour for the means necessary to give them and their distant families the barest of livings. No modern nation, even in the face of the direct military necessity, could maintain such numbers in the field. Certainly it would not be willing to maintain such a force outside its borders in peacetime. The social, medical, economic, and moral results of this migratory labour are catastrophic, and the system cannot be condemned too strongly.

The incidence of venereal disease is high amongst Africans in those areas where European civilization and industry have become firmly established. The published figures are in fact staggering when compared with those from other areas. It is undoubted that the introduction, spread, and high incidence of syphilis amongst the native peoples of Southern Africa is directly related to contact with the European and his industry, served by migratory labour. Apparent also is the lack of attention paid to the warnings of those medical men whose writings provide the evidence of this (Kark, 1949; Sax, 1952). The excellent survey of the social pathology of syphilis in Africans by Kark (1949) presents the facts admirably. To combat the amount of venereal disease now in existence in certain areas demands an extensive organization of social, medical, and educational workers. Moreover, the essential features of migratory labour among backward peoples are such as to prevent any effective control by such measures. Effective legislative measures to prevent the spread of disease can be placed on the statutes, and exist, but to put such measures into effect would result in social, economic, and legal chaos.

Malnutrition

The increasing dependence of the native in the reserves upon migratory labour, his ignorance of proper farming methods, and its sequelae—neglect, overstocking, and soil erosion and exhaustion—combined with a natural increase in population, have produced an intense and increasing problem of malnutrition. Unless checked this of itself is likely to have far-reaching effects, and it is already taking its toll. The selective action of malnutrition on the native female of the reserves has been noted (Jackson, 1952). That a process of racial degeneration due to malnutrition may be taking place can be supported by reasoning alone, and has been suspected (Gillman and Gillman, 1951; Jackson, 1952; Jones, 1952). Two processes are probably involved.

(*a*) The fertilized ovum is to some extent independent of the mother, even while *in utero*, and makes every effort to satisfy its own biological demands for development and growth. The high incidence of miscarriage and premature birth among malnourished African women is known (Gillman and Gillman, 1951; Ross, 1952). That the high abortion rate can be solely attributed to venereal disease is doubtful. It is conceivable and highly probable that the genetically larger foetus with a greater biological demand will be unable to satisfy its needs from a malnourished mother and consequently will undergo foetal death and be lost through abortion. This process, if operative, is likely to be highly selective under intensive malnutrition and will be a potent factor in racial degeneration.

(*b*) The summation from generation to generation of the environmental influence of diet in man where there is a long gestational period must also play a part in general somatic deterioration. It must be remembered that the predominant part played by carbohydrate, and particularly by maize in certain areas, is conducive to degenerative changes in the mother and possibly in her infant.

Malnutrition in the native results in a high incidence of preventable disease. This includes premature ageing, tuberculosis, skin infections, general inefficiency, and backwardness. The most important single factor contributing to the high incidence of tuberculosis in the African is malnutrition. The incidence of tuberculosis in the native of Southern Africa is the highest in the world. In areas where maize is the staple article of diet insanity is a sequel to the malnutrition, and the insidious mental degeneration consequent upon such a diet must contribute to general mental backwardness of the people.

It has often been said that African labour is not cheap. This statement is true because the labour is inefficient and there is a high wastage, but it needs qualifying by an assessment of the medical and social handicaps which contribute to the inefficiency. Too much has been expected of the African. One is surprised, taking all circumstances into consideration, that he has accomplished, and continues to accomplish, as much as he does to-day.

Detribalization

There is growing up in Southern Africa a class of men often referred to as detribalized natives. They are most numerous in the towns, but their counterparts are beginning to appear in the reserves. The term is used frequently with an implication of regret and depreciation, as though they were social misfits. This is strange. In actual fact they are the natural products of civilization and industrialization and will appear wherever the natives are employed by industry. Upon them will turn the fate of Africa. The tragedy of Southern Africa to-day is that the logistics of their advent played no part in the development of the country. There is to-day an amorphous mass of human material living without tradition, social structure, or allegiance in slum conditions exhibiting the worst forms of human degradation, poverty, malnutrition, and disease. These masses have grown up around all the large European residential and industrial centres. There was no planning, and the problem is practically out of control. From these areas have radiated social diseases which have contaminated the most distant tribes (Kark, 1949; Sax, 1952).

The detribalized natives are in an unenviable and tragic position, for no place was made for them, and their natural heritage has been denied them. No attempt has been made to guarantee them a social structure and a feeling of belonging to a society within the natural order of their existence. As a group they are without a name or a home.

A Problem for the Future

From the foregoing and from the literature quoted an investigator will obtain the impression, and rightly so, that the progress of civilization in Africa has resulted, so far, in a progressive burden of social maladjustment, disease, poverty, and malnutrition for the African people. One might say that if the African is suspicious of the intentions of European civilization he is, judging by the results, justified from a medical point of view.

In any discussion of social medical problems, particularly concerning a continent of multiracial and multitribal inhabitants, it is difficult to avoid confusing politics and preventive medicine. I doubt, in actual fact, whether they can be dissociated, unless the discussion of the problems outlined be regarded as education of the races involved on the nature of the prospects before them. One thing is certain—that for the safety and economic prosperity of the African continent capital and labour from all races must combine to produce harmony and to avoid the potential dangers which lie ahead. For those territories which are yet undeveloped, planning will ensure a stability and prosperity which will exceed anything yet accomplished in the continent. The

prosperity of any section accomplished at the expense of the legitimate human needs of another, at the expense of the soil, or of any other resource, is exploitation and will finally result in chaos. There may or may not be a remedy. The economic drain of preventable disease, both social and secondary to ignorance, poverty, and malnutrition, will, unless checked, prove a burden eventually on any society. In a multiracial interdependent society its results in one section are likely to be disastrous for all. It is apparent from the literature quoted that members of the medical profession are concerned about the medical prospects in Africa. To adopt the attitude that everything will come right in the end in areas where such conditions exist is an admission of defeat. In areas where it does not exist but may arise such an approach would be tantamount to negligence.

The future of Africa is the heritage and the responsibility of all races within its bounds. The problems are theirs.

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MEDICAL NEW YEAR HONOURS

The names of the following members of the medical profession were included in the New Year Honours List published in the *London Gazette* on January 1.

G.C.V.O.

LORD WEBB-JOHNSON, K.C.V.O., C.B.E., D.S.O., T.D., M.B., Ch.B., F.R.C.S. President of the Royal College of Surgeons of England, 1941–9.

Knighthood

EDWARD CHARLES DODDS, M.V.O., M.D., Ph.D., D.Sc., F.R.C.P., F.R.S. Courtauld Professor of Biochemistry, University of London.

ERIC WILFRED FISH, C.B.E., M.D., D.Sc., F.D.S. Chairman of the Dental Board of the United Kingdom since 1944.

FREDERICK TAVINOR REES, C.B.E., *M.C.*, T.D., M.R.C.S., L.R.C.P. Lately Director-General of Medical Services, Ministry of Pensions.

BRIAN HERBERT SWIFT, *M.C.*, M.D., F.R.C.S.Ed., F.R.A.C.S., F.R.C.O.G. In recognition of his valuable services to public hospitals and to the University of Adelaide.

HARRY WYATT WUNDERLY, M.D., F.R.C.P., F.R.A.C.P. Director of Tuberculosis, Commonwealth Department of Health, Canberra.

C.B. (Military Division)

EDWARD PHILIP NAGLE CREAGH, M.B., B.Ch., M.R.C.P. Major-General, late R.A.M.C. Honorary Physician to the Queen.

VYVYAN STEWART EWING, C.B.E., M.B., Ch.B. Air Vice-Marshal, R.A.F.

WILLIAM RALSTON DUNCAN HAMILTON, O.B.E., M.D. Major-General, late R.A.M.C. Honorary Physician to the Queen.

ROBERT WALSH MUSSEN, C.B.E., M.D., F.R.C.P. Surgeon Rear-Admiral.

C.B. (Civil Division)

GEORGE ALBERT CLARK, V.R.D., M.D. Principal Medical Officer, Ministry of Health.

C.M.G.

HUGH WADDELL MULLIGAN, M.D. Colonel, late R.A.M.C. Director, West African Institute for Trypanosomiasis Research, Colonial Research Service.

WALTER GERALD WICKREMESINGHE, O.B.E., M.R.C.S., L.R.C.P. Lately Acting Director of Health Services, Ceylon.

C.V.O.

WILFRID PERCY HENRY SHELDON, M.D., F.R.C.P.

WILLIAM ELDON TUCKER, M.B.E., T.D., M.B., B.Chir., F.R.C.S.

C.B.E. (Military Division)

CHRISTOPHER CROWLEY, M.B., B.Ch., D.P.H. Group Captain, R.A.F.

ROBERT JAMES ROSIE, M.B., Ch.B. Brigadier, late R.A.M.C. Honorary Physician to the Queen.

ERIC THOMAS SUTHERLAND RUDD, M.B., B.Ch., F.R.C.S.Ed. Surgeon Captain, R.N.

CAMPION AUBREY RUMBALL, O.B.E., F.R.C.P., D.T.M.&H., D.P.M., L.D.S. Air Commodore, R.A.F. Honorary Physician to the Queen.

C.B.E. (Civil Division)

CYRIL JOHN AUSTIN, O.B.E., M.B., Ch.B. Lately Medical Superintendent, Leprosy Hospital, Makogai, Fiji.

KATE ISABEL CAMPBELL, M.D. For services to medical science in Australia.

WILLIAM GEORGE CLARK, M.B., Ch.B., F.R.C.P.Ed., D.P.H. Lately Medical Officer of Health, Edinburgh.

JAMES THOMAS CURRAN, M.B., Ch.B. Group Physician Superintendent, Lennox Castle and associated institutions, Lennoxtown, Stirlingshire.

THOMAS HALL JAMES DOUGLAS, F.R.F.P.S., Hon. F.D.S. Chief Dental Officer, Department of Health for Scotland.

THOMAS FERGUSON, M.D., D.Sc., F.R.C.P.Ed., F.R.F.P.S., D.P.H. Professor of Public Health, University of Glasgow.

CHARLES MONTAGUE FLETCHER, M.D., F.R.C.P. Physician and Senior Lecturer, Postgraduate Medical School of London.

MUSTAPHA BIN OSMAN, M.B. State Medical and Health Officer, Kedah, Federation of Malaya.

O.B.E. (Military Division)

JOHN MORLEY HOLFORD, M.B., B.Chir., M.R.C.P. Surgeon Commander, R.N.

EUSTACE ALWYNNE ROWLANDS, V.R.D., M.B., B.S., F.R.C.S., F.R.A.C.S. Surgeon Commander, Royal Australian Naval Reserve.

DAVID WRIGHT, D.S.O., M.B., Ch.B., F.R.C.S.Ed., Lieutenant-Colonel, R.A.M.C. In recognition of non-operational services in Japan in connexion with operations in Korea.

O.B.E. (Civil Division)

WILLIAM ARTHUR ANDERSON, M.B., Ch.B., J.P., of Queenstown, New Zealand. For services to the community.

GEOFFREY OSBORN BARBER, M.B., B.Chir. Lecturer in General Practice, St. Mary's Hospital Medical School.

LOUIS GERARD BLAZÉ, L.R.C.P.&S.Ed. Lately Acting Deputy Director of Health (Medical Services), Ceylon.

REGINALD MURRAY DUNSTONE, M.B., Ch.B., J.P. For public and social welfare services in the Commonwealth of Australia.

MACORMACK CHARLES FARRELL EASMON, M.D. Senior Medical Officer, Sierra Leone.

DENNIS HERBERT GEFFEN, M.D., D.P.H. Medical Officer of Health, St. Pancras and Hampstead.

JOHN THOMSON GUNTHER, M.B., B.S. Director of the Department of Public Health of the Territory of Papua and New Guinea.

GOPAL HARIDAS, M.D., M.R.C.P. For services to the St. John Ambulance Brigade and movement in Singapore.

SAMUEL HORTON OLUWOLÉ JONES, M.B., Ch.B., D.T.M.&H. Colonial Medical Service. Director of Medical Services, Gambia.

JOHN WILSON MCCAGIE, L.R.C.P.&S.Ed., L.D.S. Lately Senior Medical Officer, Ministry of Pensions.

VATAPAKAT RAMANMENON NARAYANA MENON, M.B., B.S. Medical Officer, Dindings, Federation of Malaya.

The Reverend Sister MARGARET MARY NOLAN, M.Ch., M.A.O., F.R.C.S.I., F.R.C.O.G., D.T.M.&H., D.P.H. For medical and missionary work in Nigeria.

BERTIE SOUTAR SIMPSON, M.B., Ch.B., F.R.C.S.Ed., J.P. Consultant Surgeon for the County of Sutherland.

JAMES ANDERSON SMILEY, M.D., D.I.H. Factory doctor for East Belfast. Special Lecturer in Occupational Health and Lecturer in Forensic Medicine, Queen's University, Belfast.

HENRY GEORGE TRIAY, M.D., D.C.H. For medical services in Gibraltar.

HUBERT CAREY TROWELL, M.D., F.R.C.P. Colonial Medical Service Specialist (Physician), Uganda.

WILLIAM HENDERSON WATSON, M.D. Medical Officer in Charge, Mental Hospital, Nyasaland.

M.B.E. (Military Division)

ANTHONY ST. CLAIR REX DE COSTA, M.B., B.S. Captain, Ceylon Volunteer Force.

CHRISTOPHER BERKELEY WYNN-PARRY, B.M., B.Ch., D.Phys.Med. Acting Squadron Leader, R.A.F.

M.B.E. (Civil Division)

RATU JIONE ANTONIO RABICI DOVI, M.B., Ch.B. Medical Officer, British Solomon Islands Protectorate.

VISHNUPRASAD BALKRISHNA PANDIT, L.C.P.S. Senior Sub-Assistant Surgeon, Uganda.

ETHEL JOYCE SAWARD, M.R.C.S., L.R.C.P. For medical services in Jamaica.

CHARLOTTE ANNIE STUART, M.B., B.Ch., D.T.M.&H. Principal Medical Officer, Church Missionary Society Hospital, Cairo.

RAPHAEL LAWRENCE TIRUCHELVAM, M.R.C.S., L.R.C.P., D.T.M.&H., D.P.H. Acting Director of Social Services, Ceylon.

ARTHUR STANLEY WINT, M.B., B.S. For services to sport in Jamaica.

Kenneth Mellanby, Sc.D., who was appointed O.B.E. in 1945, has been promoted to Commander of the Order of the British Empire in the New Year Honours List. He has recently relinquished the post of Principal of University College, Ibadan, Nigeria, to which he was appointed in 1947.

Nova et Vetera

BATTLE OF EPONYMY

Eponymous structures in anatomy may sometimes give trouble. For on occasion the structure may be named after a person who does not deserve such a chance to immortality, or the structure as originally described is quite different from the current view. The common description of Hesselbach's triangle is a triangle delimited by the inguinal ligament below, medially by the lateral edge of the rectus abdominis muscle, and laterally by the fold of peritoneum raised by the inferior epigastric artery. Such a triangle is described in the first edition of Jones Quain's *Elements of Descriptive and Practical Anatomy*, London, 1828, immediately after mentioning Hesselbach's name with regard to hernia externa or indirect inguinal hernia.

In fact, however, Franz Caspar Hesselbach (1759–1816), professor of surgery at Würzburg, in his *Anatomisch-Chirurgische Abhandlung über den Ursprung der Leistenbrüche*, Würzburg, 1806, and more clearly in 1814,[1] originally described the triangle differently. His definition, which is clarified in the plates, was a triangle bounded below by the horizontal ramus of the pubic bone, medially by the lateral edge of the rectus abdominis muscle, and laterally by the femoral vein and inferior epigastric artery. He distinguished external and internal (direct) inguinal herniae and femoral herniae, and described the abnormal obturator artery. Hesselbach pointed out that the two lower corners of the triangle he described were important, and gave his reasons. The medial corner, between the margin of the rectus abdominis and the pubis, where the abdominal wall is weakened by the superficial inguinal ring, is the site of origin of a direct inguinal hernia. The lateral corner, between the pubic ramus and the femoral vein, is the site of the neck of a femoral hernia. In view of this precise statement it is strange how the modern view of the triangle arose and how early the change was made.

Hesselbach is usually given the distinction of having been the first to define the difference between indirect and direct inguinal herniae, but Astley Cooper[2] in 1804, and two years earlier than Hesselbach's book, quoted the London surgeon, Henry Cline (1750–1827) as having made the observation in his surgical lectures at St. Thomas's and Guy's Hospitals in 1777. A search through five manuscripts of students' notes of Cline's lectures, one dated 1785 and another 1791, at the Royal College of Surgeons has confirmed this. Astley Cooper also confirmed the observation from his own experiences.

In the 1806 book Hesselbach mentions another name for the inguinal ligament—the ligament of Fallopius. Joseph Hyrtl (1810–94), professor of anatomy at Vienna, in his *Onomatologia Anatomica*, Vienna, 1880, has a comment on this. "I do not understand why the structure, which was known by Vesalius (Book 2, chapter 31, of the *Fabrica*, 1543) and excellently described by Fallopius (an Italian anatomist, 1523–63) in his *Observationes Anatomicae*, Venice, 1561, between the iliac spine and the symphysis pubis is called 'ligamentum Poupartii.' François Poupart (a French surgeon, 1661–1709) had the temerity or ignorance to describe this ligament as something new, thus earning the gratitude of his compatriots." However, 90 years earlier, a Frenchman, Antoine Portal (1742–1832), who on the title page of his *Histoire de l'Anatomie et de la Chirurgie*, Paris, 1770, is described as "lecteur du Roi, Professeur de Médecine au Collège Royal de France, Professeur d'Anatomie de Monseigneur le Dauphin, de l'Academie Royale des Sciences, etc., etc.," had already written in favour of Fallopius's name for this ligament: "C'est ce ligament que l'ignorance a fait attribuer à Pourpart, qui a vécu cent ans après: quelle erreur! quelle faute d'histoire! des Anatomistes modernes, fameux d'ailleurs, sont cependant sujets à de pareilles méprises." Despite this, for many years it has been Poupart who has usually won what might be called this international battle of eponomy.

My thanks are due to Professor J. D. Boyd and Mr. W. Le Fanu, Librarian at the Royal College of Surgeons, for their help.

MILO KEYNES.

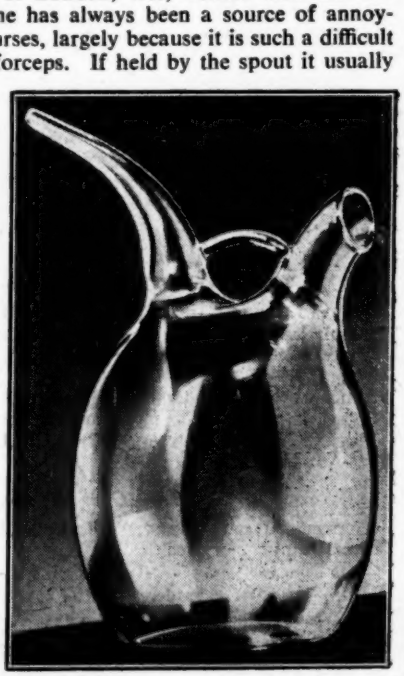
[1] *Neueste anatomisch-pathologische Untersuchungen über den Ursprung und das Fortschreiten der Leisten- und Schenkelbrüche*, Würzburg, 1814.

[2] *The Anatomy and Surgical Treatment of Inguinal and Congenital Hernia*, London, 1804.

Preparations and Appliances

AN IMPROVED UNDINE

Mr. L. G. SCOULAR, of London, W.1, writes: The sterilization of a glass undine has always been a source of annoyance to sisters and nurses, largely because it is such a difficult thing to grasp with forceps. If held by the spout it usually breaks, and if the inlet is grasped the nurse has her fingers scalded by the boiling water, which runs down the forceps as she inverts the undine. The photograph shows an undine which Messrs. Clement Clarke, of Wigmore Street, London, W.1, have made for me. The chief feature is a bridge or handle between the spout and the inlet. By this it can be held with forceps, picked out of a boiling sterilizer, and inverted. It is of uniform size, and contains 5 fl. oz. (140 ml.). There is a wide base to give it stability, and the inlet points outwards rather than upwards so as to minimize the collection of dust. Being made of "pyrex" glass, it is stronger and has greater thermal resistance than those made of ordinary glass.



Correspondence

Because of the present high cost of producing the Journal, and the great pressure on our space, correspondents are asked to keep their letters short.

Radiology and Lumbar Disks

SIR,—The review in your leading article (*Journal*, December 19, 1953, p. 1363) entitled "Radiology and Lumbar Disks" gives an excellent picture of current attitudes towards the diagnosis of this fashionable complaint. In the same issue under "The Doctors' Diseases" (p. 1372) you report Mr. E. A. J. Heath as saying that in the experience of an insurance company the diagnosis of prolapsed disk was on the increase. He further stated that the condition showed a considerable augmentation of the period of disability when compared with that due to lumbago, sciatica, and sacro-iliac strain in 1937. I could therefore have wished your survey might have extended to assess the results of treatment based on the newer aetiology.

Most clinicians, especially those whose experience stretches back 30 or 40 years, would agree that, up to date, the human race has not benefited as much as might have been hoped from the demonstration of the mechanical cause of several conditions previously incorrectly labelled. I can say that among the Metropolitan Police the period of disability or incapacity from complaints diagnosed or suspected as being due to prolapsed disk conforms to the figures given by Mr. Heath.

If these statements are accepted, they appear to offer a challenge to our current methods of managing the condition. The answers will no doubt vary. I agree that now that the first enthusiasm for operation has passed the selection of cases which justify surgery is slowly finding its level. In the less severe examples without gross neurological signs two factors may be responsible for causing unnecessarily prolonged disability. The first is premature diagnosis. Many practitioners are all too ready to attribute "lumbago" or "fibrositis" of the buttock to prolapsed disk and to inform the patient of this possibility. A hospital assignment is the natural sequence. Often enough I am faced with a policeman who appears to be fit for duty after an attack of lumbago: in accordance with his sensibility to a diagnosis which suggests that there is something radically wrong with his spine he may or may not agree. Frequently, however, he says: "Oh, I have an appointment next week to have an *x*-ray and see a specialist," and, not unreasonably, he thinks he should remain on the sick list. The second factor is the commonly prescribed system of treatment for fairly severe cases. I am inclined to think that prolonged partial immobilization in plaster followed by the provision of a restrictive belt is a too frequent routine. It seems that limited rest, traction, and exercise to restore muscle tone and function are not as generally employed as they might be.

Whatever value may be attached to my suggestions I would submit that we should recognize that, though the aetiology of sciatica and the like may be established, the resultant form of treatment has, up to date, been productive of as much, if not more, harm than good to the community.—I am, etc.,

Faversham, Kent. MAX PAGE.

SIR,—May I be permitted to comment on your leading article, "Radiology and Lumbar Disks" (*Journal*, December 19, 1953, p. 1363)? After careful study I found it difficult to decide whether it contained a plea for the more extensive use of myelography, and concluded that this was probably the case. It seemed to be based upon the need to exclude—or reveal—the presence of a tumour in patients suspected of suffering from a protruded lumbar disk. The incidence of tumours misdiagnosed as protruded disk, according to the quoted figures, was 4.3% at the Lahey Clinic and about 8% at the Mayo Clinic. But these cases were nevertheless dealt with by operation—presumably satisfactorily. Would the writer recommend myelography in every case of suspected lumbar disk protrusion in order to demonstrate pre-operatively tumours in those patients ultimately brought to operation? If that be the case, since the writer makes the statement (and many would agree with it) that "four out of five cases get better when treated conservatively," myelography would be carried out for a condition which occurs in probably not more than 1% of the cases. The statement is made that there is a prejudice against myelography in many centres in Britain, especially amongst orthopaedic surgeons. This is a most fortunate "prejudice" and the use of this word perhaps implies the writer's leaning towards this procedure. He states later that at most neurological centres myelography is held to be an essential investigation; I can hardly credit this, and wonder on what experience he bases such an opinion. And *essential* in which cases?

Finally, he quotes Barr that *catastrophes* can only be avoided by *routine myelography*. Is this closing remark a recommendation? If so, it needs critical examination. What are the catastrophes to be avoided? Those which arise from a lack of careful assessment of the history (so often neglected) and physical signs? A routine investigation—in all patients complaining of posterior crural pain, or of those coming to operation with a carefully considered diagnosis? It would be a retrograde step if, after "twenty years" of experience, those who treated patients were to employ as a routine a procedure which (with present contrast media) is not without danger, is not entirely reliable for the diagnosis of lumbar disk protrusion, and is usually redundant. One had hoped that in this country medicine had now achieved a more critical outlook. Myelography is a valuable method of investigating the spinal canal, and it may be helpful in the investigation of a small proportion of cases of suspected lumbar disk protrusion. The quickest way of bringing it into disrepute is to use it as a routine procedure.—I am, etc.,

London, E.1. D. W. C. NORTHFIELD.

SIR,—Your leading article on radiology and lumbar disks (*Journal*, December 19, 1953, p. 1363) leads me to believe that nobody in Britain has yet seen fit to put on trial the methods described by Hasner, Schalimtzek, and Snorrason.[1] These gentlemen, working at the State Hospital, Copenhagen, have evolved what they call a functional *x*-ray examination of the spine, and, as its name implies, the rationale is to examine the spine radiologically from a functional point of view—namely, in its main positions of flexion, extension, and lateral bending. In the first two positions the films are taken in the lateral view, whilst in the third position they are taken in the antero-posterior view.

When the normal spine bends in whatever direction, the vertebrae angulate on each other, the angles converging to the concavity of the spine. In cases of prolapsing or degenerating disk there is either parallelism of the vertebral bodies or paradoxical angulation—i.e., the angle formed between the two vertebrae converges to the convex side of the spine. In a series of 90 cases these workers were able to demonstrate 86 abnormal disks by their functional *x*-ray examination. Of 13 patients submitted to operation the functional *x*-ray findings were confirmed in 12, whereas straight *x*-ray only revealed 6 cases. In this same series of 13 cases, myelography failed to reveal one case which the functional *x*-ray discovered, and vice versa.

I would have thought that there was sufficient evidence of the merit of this method to warrant its being taken up in this country.—I am, etc.,

Salford, 7. HYMAN DAVIES.

REFERENCE

[1] *Acta radiol. (Stockh.)*, 1952, 37, 141.

SIR,—In your leading article on radiology and lumbar disks (*Journal*, December 19, 1953, p. 1363) you state that an enormous "disk" literature has grown up in the past 20 years and that opinions still differ widely on diagnosis, treatment, and prognosis. However, there is one aspect of

this disorder on which there is complete agreement, that is the gross severity of sciatic pain. For this reason I would like to suggest a rapid method of treatment that requires no particular manipulative skill.

The problem of replacing a herniated disk, as I see it, is to reduce the intervertebral pressure below the level of that exerted by the tissues on the displaced disk. Intervertebral pressures are evidently at their lowest when there is full adaptation for muscular activity. The initial response to an effort stimulus is an extensor movement. This includes contraction of the erectores spinae muscles—bracing oneself for an effort, as it is usually known. The movement is a sustained contraction but is, none the less, a movement. The spinal column is thus extended and supported, and strain is distributed evenly along the whole column. On the other hand, intervertebral pressures are probably at their highest when the extensor muscles are relaxed. Anybody who has had the experience of heading a ball relaxed, or "flatfooted" as it is called, is unlikely to forget the jarring sensation along the spine and sacro-iliac joints. No such effects ensue when one "goes up" to the ball. With full extension the muscles take over the burden of the joints. For a like reason it is less fatiguing to walk for an hour than to stand still for a quarter of that time. When the extensors are relaxed the spine is flexed and the intervertebral pressure tends to be greater at the anterior aspect of the disk. Physical effort, such as lifting a weight, without the preliminary protective extensor contraction will increase the pressure on the anterior portion of the disk and retropulsion is liable to occur. In other words the immediate or precipitating cause of disk displacement is the failure of the patient to react in a normal way to an effort stimulus.

The treatment then is to restore the initial extensor response. The patient lying in the prone position is encouraged to extend the lower limbs and contract the plantar muscles. He is then asked to raise his head (without arm help) and at the same time to expirate fully. Expiratory movement synchronizing with the initial extensor movement is the normal respiratory response to an effort stimulus. The diaphragm should be relaxed as much as possible. My manipulative reinforcement of these extensor efforts on the part of the patient is merely to raise the sciatic limb slightly at the knee and at the same time to apply moderate pressure of a few seconds' duration to the lumbo-sacral region. One such attempt at disk replacement is sufficient. I have had no failure in the few cases I have experimented on. In fact I believe it possible for a determined, fully co-operating patient to replace a disk without any manipulative help. The earlier the patient is treated the better and quicker the results.

This method of treatment can do little harm in the 5–8% of cases of sciatica due to tumours—usually of the benign type. As for the occasional tubercular cause, a careful history and clinical investigation should be of help. An additional safeguard in this type of case would be the failure of the patient to co-operate—the extensor response being rather feeble in tubercular subjects—in other words, no co-operation, no manipulation.—I am, etc.,

Callan, Co. Kilkenny. WILLIAM HERON.

Ulcerative Colitis

SIR,—I was much interested in Mr. Stanley O. Aylett's article on the surgery of ulcerative colitis (*Journal*, December 19, 1953, p. 1348) and in the annotation on that subject in the same issue of the *Journal* (p. 1364). Ileostomy, of course, is a beastly operation and Mr. Aylett is to be congratulated on having devised a substitute for it. But what has happened to appendicostomy? Time was when I saw quite a number of cases of ulcerative colitis of all degrees of severity, and my experience was that an appendicostomy followed by lavage of the colon with saline was far the best treatment. The operation was usually done by Mr. Lockhart-Mummery, and many of the patients wore a tube for months or even years, washing out the colon as required and meanwhile carrying on their ordinary vocations in perfect comfort. I think the results were quite as good as those claimed by Mr. Aylett.

Why, then, has the operation fallen into disuse? It can hardly be, as apparently is the case with gastro-enterostomy, that the modern surgeon has lost the "know how" (to use a horrid Americanism) of it, for the technique is really quite simple. It is, perhaps, merely a case of going out of fashion, there being, as we all know, fashions in operations just as there are in women's hats. Or has appendicostomy joined the ghostly company of "forgotten treatments" about which I have often thought a valuable essay might be written by someone willing to wade deep enough into the morass of old medical literature? Perhaps Mr. Aylett or some other active abdominal artificer will kindly enlighten me.

As to the statement in the annotation that "it is now widely recognized" that sufferers from ulcerative colitis "are people characterized by emotional immaturity, often having a pathological parental attachment," I can only say, "Dear, dear, who'd have thought it?" That such a distressing malady can induce mental disturbances is understandable, for has it not been said that nothing saps the morale of an army more than an epidemic of dysentery, but that a pathological parental attachment can cause, or even predispose to, ulcerative colitis demands more credulity than I, at least, possess. Is this not another example of the tendency in the modern concept of psychosomatic disease for the "psycho" element to steal the limelight from the somatic?—I am, etc.,

Streatley, Berks. ROBERT HUTCHISON.

SIR,—The article on the conservative surgery of ulcerative colitis by Mr. Stanley O. Aylett (*Journal*, December 19, 1953, p. 1348) is of particular interest to me because I have been treating these cases by the method described by Devine[1] since 1950. The results have also been completely satisfactory, with the one exception in which there was a preoperative rectal stricture. This still needs regular dilatation and there has recently developed a superficial anal fistula.

In his original article, Devine maintained that stricture was not a contraindication because by this method (a spur crushing technique between low rectum and terminal ileum) the stricture could be eradicated by the fact that half its circumference would then consist of normal ileum. Mr. Aylett's point concerning future inflammatory troubles in this type of rectum is borne out by this case, who otherwise is a happy, healthy young woman soon to be married (a point considered in choosing her original surgical procedure). My other five cases, which were all cases referred by physicians because of chronicity, colonic stricture, pyodermia, and, in one case, multiple arthritis and profound toxaemia, are now all well with an average of two to three bowel movements per day and, when last examined, a healthy rectal mucosa.

I have found that, by leaving a long devitalized loop on the proximal ileum and using this to drain the ileal content via a Paul's tube, and by applying the spur crushing clamp through the open rectal stump and a small hole in the ileum just proximal to the gangrenous loop on the second post-operative day, the spur can be obliterated very early, even while the loop is still draining most of the ileal content clear of the abdominal skin. Aluminium paste, hexamethonium, and early closing of the open ileo-rectal stoma on the fourteenth post-operative day are all aids in getting an early rectal defaecation.

There is no doubt that by this technique and by using an extensive mobilization of the rectum a much more complete colectomy can be subsequently performed. One reads of criticisms of this method in which the critic describes "having to undo the ileo-sigmoid anastomosis" before establishing ileostomy. This declaration, I have always felt, reveals in part the cause of dissatisfaction which has resulted in criticism.—I am, etc.,

Great Yarmouth. H. A. MCDONALD.

REFERENCE

[1] *Postgrad. med. J.*, 1950, 26, 308.

Malaria in Ex-Servicemen

SIR,—Although Dr. C. F. J. Cropper's suggestion (*Journal*, December 5, 1953, p. 1269) for the standardization of the treatment of malaria may be acceptable to some, one rather fears that those doctors with experience of tropical diseases will question his inclusion of vomiting amongst the cardinal signs of this disease. The admitted difficulty in diagnosis surely arises from the fact that there is frequently no

cardinal sign. Otherwise how can one account for the amount of research on diagnosis which is still going on, and is still being published in the medical press of the world?

However, if we are to standardize treatment, let us also standardize the diagnosis without the awkward nautical feat of stressing cardinal points, while remembering—with vomiting—*inter alia* the work of Paladini[1] in diagnosis: "Malaria diagnosis by contraction of the muscles of the face during abdominal palpation."—I am, etc.,

Dublin. H. B. WRIGHT.

REFERENCE

[1] *Rass. Clin. Ter.*, 1929, **28**, 168.

Infection and Poliomyelitis

SIR,—With reference to your leader (*Journal*, December 5, 1953, p. 1258) upon the above-mentioned subject, the evidence which you quote from American sources that the virus of poliomyelitis is spread by close contact, and that the path of its spread is narrow, has been shown by me to be true in this country.

An epidemic of acute poliomyelitis occurred in a rural area of Kesteven, Lincs, in 1950, and involved 99 confirmed cases with 13 deaths.[1–5] It was shown that, whereas the spread of poliomyelitis had formerly been attributed to many causes—i.e., to droplet infection or to infected water and foods, milk, ice-cream, etc.; by public swimming baths; by flies; infected dust or dried excreta; by fingers and the communal use of articles recently contaminated by infectious secretions or excretions, or defective personal hygiene—this outbreak in Kesteven demonstrated beyond all doubt that the predominant method of spread of poliomyelitis is by personal contact via the respiratory route.

In all, 114 cases were notified (99 corrected) mostly in the third quarter of 1950. The epidemic originated in the village of Digby (population 1,134), in the rural district of East Kesteven, which had 16 cases. Eleven days after the onset, the disease spread to an adjoining village where 10 cases occurred. Three days later nine cases began to be notified in another village 1½ miles from Digby. In the second fortnight of the outbreak seven more villages were affected, all within four to five miles of Digby. In the third fortnight three other villages were involved, while in the fourth fortnight two more villages were attacked by the disease.

That poliomyelitis was spread in this outbreak by personal contact with infectious persons was proved by the transport of infection between villages over bus routes. All the confirmed cases were resident on organized bus routes, there being no other common mode of transport; some were known to have travelled by bus during the incubation period of the disease. Detailed inquiries showed that there were also links, direct and indirect contacts, between many of the cases, extending over a wide area. In a very high proportion of those affected with poliomyelitis, close personal contact with a declared case or infected household was established.

In the last paragraph of your leading article, in relation to the control of poliomyelitis, you state that quarantine of contacts is the obvious attack, but, if this is to be effective, contact with other people must cease. Doubt is expressed as to whether the movements of adults should be restricted compulsorily, if in fact this can be done at all. I agree that the movements of adult contacts may be difficult to control, especially in city life. Further, there are no restrictions in law upon the movements of such contacts. However, in an article in *The Medical Officer*[3] I gave details of the comprehensive measures, including restrictions upon child and adult movement, which were adopted during the Kesteven epidemic. As a measure of their efficacy it is of interest to record the fact that this epidemic was confined to the rural district where it originated and did not spread to other parts of the county.

It is true that much can be done on a voluntary basis by supervision of contacts by trained staff, publicity, and informed public opinion to control this disease, as implied in your leading article. In particular, since close personal contact has been shown to be the predominant factor in the spread of this disease, the M.O.H. and his colleagues in general medical practice will in future be in a better position to give appropriate advice with regard to prevention. Moreover, valuable time may be saved to the M.O.H. in the early stages of an outbreak, as it may not be necessary, unless he has special reasons, for him to devote time to investigations, which are likely to prove futile, into the possibility of water, food, etc., having been the vectors of infection.

When a serious outbreak of poliomyelitis occurs, it is quickly brought to the notice of the public in the area concerned that they are being attacked by a disease which paralyses or kills. In view of the great amount of press publicity, local and even national, which is given to this aspect, the active co-operation of adult contacts, as well as parents of child contacts, and the public at risk, is not difficult to secure with regard to all precautions which should be taken.—I am, etc.,

Sleaford, Lincs. J. H. C. CLARKE.

REFERENCES

[1] *Annual Report of the M.O.H. County of Lincoln—Parts of Kesteven*, 1950, p. 7.
[2] *Med. Off.*, 1951, **86**, 167 and 171.
[3] *Report of the Ministry of Health*, April 1, 1950, to December 31, 1951, p. 36. H.M.S.O., London.
[4] *Lancet*, 1951, **2**, 1129.
[5] *County Councils Association Official Gazette*, 1952, November, p. 193.

A Cosmetic Amputation

SIR,—Sir Heneage Ogilvie (*Journal*, December 12, 1953, p. 1322), referring to the amputation of the index or little finger along with part of the metacarpal, rightly condemns this operation in the manual worker. Obviously, where breadth of hand is an important factor in a man's ability to grasp large objects, the loss of the metacarpal head reduces his working capacity. On the other hand, where a patient's employment calls for the minimum of disfigurement, the gradual tapering produced by the oblique section through the metacarpal is much less noticeable than the abrupt stump produced by disarticulation at the metacarpal phalangeal joint.

If the oblique section is carried out with good plastic surgical technique, there is no reason why the scar should limit the movements of the adjoining finger, or remain tender for an abnormal length of time. These faults suggest technical errors. If sufficient padding of subcutaneous fat and interosseous muscle is left to cover the cut surface of the metacarpal, and the scar is placed towards the dorsal surface, no limitation of movement should result. Neuromata rarely develop if the digital nerves are shortened and allowed to retract well into the soft tissues, where they will not be exposed to pressure or friction. Tenderness and retraction of the scar are complications which arise when the latter is placed too much toward the volar surface or has become adherent to the cut surface of the bone.

Our practice in every case is to discuss with the patient the relative merits of the two operations in relation to his or her work before coming to a decision on a matter of such importance.—I am, etc.,

Basingstoke. C. R. MCCASH.

Distinguishing a Psychopath

SIR,—Dr. A. Shepherd invites criticism of his view of the psychopath in relation to mental disease (*Journal*, December 19, 1953, p. 1379). I would differ from him a little by dividing mentally ill patients into psychotics, neurotics, and psychopaths. (Any of these patients may belong to the mentally defective group mentioned by Dr. Shepherd.) I would qualify the general classification I have given by stating that the psychotics have a disturbance principally of knowing, the neurotics of emotion, and the psychopaths of action. This classification of the symptoms of the abnormal mind is in harmony with long and well established custom in the psychology of the normal mind, which regards cognition (knowing), affection (feeling), and conation (action) as different aspects of the same process.

Any given mental illness, therefore, may present as a disturbance of knowing, feeling, or action. Some, or even most, mentally ill patients show obvious disturbance of all these three aspects of the mind; but there are many who present an apparent predominance in one aspect, and of these it is of course the psychopaths who come into conflict with the law. The judge then wishes to know if the psychopath is mentally ill. By the classification I have given, the psychopath is mentally ill. But the law does not easily accept that view and often asks, in effect: "Is this psychopath also psychotic? Has he, apart from his disturbance of normal actions, also got disturbance of knowing such as

would be covered by the M'Naghten rules? If so he can surely be regarded as mentally ill, but otherwise should he not be punished?" Dr. Desmond Curran, giving evidence before Mr. Justice Hilbery (*Journal*, November 28, 1953, p. 1224), appeared to agree with this legal view, and affirmed that a psychopath "is distinct from a person suffering from a distinct disease of the mind."

The situation is, however, illogical if we accept that abnormal behaviour can derive from a mind functioning normally. The clinician, in his own province, should, I submit, accept that a psychopath is mentally ill, even though the evidence suggests that the actions of the patient are more disturbed than his thoughts or feelings. The clinician should also, of course, try to arrive at a diagnosis of the mental illness of the psychopath, as of the psychotic or neurotic. The psychopath, for instance, may be suffering from schizophrenia, or he may be an hysterical psychopath, an epileptic, a hypomanic, or a case of paranoia. And an attempt should be made to give to each illness its appropriate treatment, even though the illness may be manifest more in action than in thought or feeling.

Nevertheless, when the psychopath comes into conflict with the law, the important question remains: "If abnormal behaviour is to be regarded as a form of mental illness, is the appropriate treatment punishment?" The answer in most cases would still appear to be, and perhaps always will be, "Yes." But it is to be earnestly hoped that treatment by punishment will not so often exclude other treatment of the ailing mind.—I am, etc.,

Leicester. C. E. H. TURNER.

Glycosuria and Hyperglycaemia

SIR,—In the article on glycosuria and hyperglycaemia (*Journal*, December 19, 1953, p. 1367) the author advocates examination of two samples of urine, the second one one and a half hours after a carbohydrate meal, as a means of distinguishing between glycosuria and the presence of reducing substances other than glucose.

It has been standard practice in the R.A.F. since about 1940 to give 50 g. glucose immediately to any patient whose urine has shown reducing substances without ketones on routine examination. A further specimen of urine is tested one and a half hours later, and if the degree of reduction is not increased it is assumed that the reducing substance was not glucose.

This extension of the principle outlined by Professor Gray has practically eliminated the former common experience of glucose tolerance tests being inflicted on patients who prove to have no glycosuria.—I am, etc.,

Aylesbury. W. P. STAMM.

Insulin Zinc Suspensions

SIR,—Dr. Ian Murray (*Journal*, December 19, 1953, p. 1377) writes that it seems desirable that both protamine zinc and globin insulins should be withdrawn and be superseded by zinc suspension insulins. But why?

The articles and letters which you have published show no real advantage in the suspension insulins, and surely it is unnecessary and wrong to plunge the diabetic community, not to mention the doctors and consultants who serve them, into the confusion of using one of seven different insulins, as Dr. R. D. Lawrence (*Journal*, November 28, 1953, p. 1215) pointed out. No doubt similar control can be obtained by both the suspension and protamine insulins, but it appears that, on the whole, more of the suspension insulins, sometimes much more, is needed. This will add to the expenses of the Health Service.—I am, etc.,

Hove. G. M. WAUCHOPE.

The Pituitary and Graves's Disease

SIR,—In his paper on the clinical trial of methimazole in treatment of thyrotoxicosis (*Journal*, December 12, p. 1300) Dr. Lindsay A. G. Davidson makes the surprising dogmatic statement: "At the present time it is generally accepted that the thyroid gland in thyrotoxicosis is producing excess thyroxine in response to stimulation by excess pituitary thyrotrophic hormone." In support of this he gives references to Samson Wright's *Applied Physiology*[1] and Means's *The Thyroid and its Diseases*.[2] In the interests of accuracy it is worth drawing attention to what these authorities actually said.

Samson Wright (p. 990) says: "The initiating factor which causes the thyroid to become overactive has not been identified, but emotional stress acting via the hypothalamus on the anterior pituitary may sometimes play a part." Also (p. 980): "It is believed by some that emotional tension causing hypothalamic overactivity leads to oversecretion of thyrotrophin and the development of Graves' disease."

Means (p. 293) states that: "The aetiology of Graves' disease is quite unknown, but one may be permitted to speculate about it." This he does (p. 553), but nowhere does he say what Dr. Davidson attributes to him.

Moreover, in an annotation of recent work entitled "Pituitary–Thyroid Relations in Graves's Disease,"[3] the gist is that the results of several quoted authorities suggest that in Graves's disease the stimulus to the thyroid does not come from the pituitary.—I am, etc.,

Cambridge. LAURENCE MARTIN.

REFERENCES

1 *Applied Physiology*, 1952. London.
2 *The Thyroid and its Diseases*, 1948. Philadelphia.
3 *Lancet*, 1953, 1, 431.

Sterilizing Ampoules

SIR,—In your issue of December 5, 1953 (p. 1269), a letter by Professor L. P. Garrod condemns the practice of "sterilizing" ampoules in disinfectant solutions. With this I am in entire agreement, particularly with regard to spinal anaesthesia. Not long ago, a new box of ephedrine was opened and an ampoule discovered with no fluid in it. The ephedrine was crystallized out on the inside of the glass. No crack or flaw was visible to the naked eye. If it is possible for this to occur, or for antiseptics to diffuse through a fault in the glass ampoule, then it is also possible for bacteria to gain entry. This may be serious enough when the contents of an ampoule are given parenterally, but it could be lethal intrathecally.

For some time past it has been my practice to wrap ampoules of cinchocaine ("nupercaine") in a swab and place it alongside the syringes and spinal needles. The whole is boiled in distilled water for half an hour, in a sterilizer kept solely for this purpose. Heavy cinchocaine, of course, is allowed to cool before injection, but light cinchocaine is left in the sterilizer so that it is at the right temperature when given. In the event of a faulty ampoule, the only disaster which can arise is the injection of sterile distilled water and the humiliation of a failed spinal. To date, no ampoules have been faulty, nor damaged by boiling, and the quality of the spinal anaesthesia has not been altered. There have been no post-spinal complications from boiled cinchocaine.—I am, etc.,

Edgware. D. RECKLESS.

Antibiotics in Bacteriaemia

SIR,—There is a statement in Dr. M. Anthony Peyman's letter concerning antibiotics in bacteriaemia (*Journal*, December 19, 1953, p. 1376) which I feel cannot go unchallenged. He says: "Thus it is perfectly possible for a patient to be cured of a bacterial infection by an antibiotic while *in vitro* tests demonstrate the organism to be insensitive to that antibiotic." While I agree that this may be true in some cases with regard to the tetracyclines aureomycin and terramycin, I have never known a case of bacterial infection with a proven penicillin-resistant or streptomycin-resistant organism be cured by these antibiotics; and I maintain that it is a waste of time and antibiotic to persist with treatment when laboratory tests show that an organism is resistant to either of these antibiotics. In general, the rule still holds that one should be guided by the laboratory tests in treating a case with antibiotics, keeping in mind that exceptions with regard to aureomycin and terramycin are possible.—I am, etc.,

Guildford. A. LAWRENCE.

Medresco Hearing-aids

SIR,—I am sure none of your readers could have been misled by Mr. A. E. Stevens's use (*Journal*, December 19, 1953, p. 1376) of the results of our inquiry.[1] He says that "only 18% of the aids issued were ever taken to work," but he omits to point out that as many as 54% of the patients do not even take *themselves* to work. Only 46% of the patients are, of course, in employment and therefore in a position to take their aids to work. In fact the report said nothing about taking aids to work. It said: "Of the Medresco users who were workers 44% used their aids *when working*." Mr. Stevens's calculation of the 18% is an excellent example of the misuse of statistics.

To correct any false impression this may have given, another sentence might be quoted from the article: "With as many as 91% of the patients claiming to understand all or most of what is said when using the aid, it is scarcely surprising to find that the service has been enthusiastically received." Perhaps we should have added—"by the patients."—I am, etc.,

London, W.C.1. P. G. GRAY.

REFERENCE

[1] *Lancet*, 1951, **1**, 1170.

Controlled Hypothermia

SIR,—I have read with great interest the two papers in the *Journal* of December 5, 1953 (pp. 1237 and 1244), on controlled hypothermia.

I think it is to be regretted that the term "cocktail" has been introduced into medical literature. Unfortunately the French have had the bad taste to make use of this expression and you may be sure that it will soon find its way into their popular press and will lend itself to cheap jokes and advertising for "cocktails" as an adjuvant in modern surgery.

British medical journals combine sobriety with humour of a subtler kind. The "cocktail" might well have been omitted from an interesting report on a new form of treatment.—I am, etc.,

Basel. ERICH ZIMMERLI.

Appendix in the Hernial Sac

SIR,—Professor Lambert Rogers (*Journal*, December 12, 1953, p. 1324) draws attention to a recent article by P. G. Creese[1] in which Claudius Amyand, of St. George's Hospital, is given due, if belated, credit for the first appendicectomy, which he performed in 1735. Some months ago in searching the *Philosophical Transactions* for early accounts of the acute abdomen I chanced on Amyand's account "of an iliac passion occasioned by an appendix in the ilion."[2] This is a clear description of the necropsy of a boy of 10 who died of peritonitis following acute inflammation of the structure later to be known as Meckel's diverticulum. It is almost certainly the first account of disease of this vestigial structure. I was so struck by this report that I looked for other case records written by Amyand and was rewarded by the discovery of his report of the successful removal of the appendix from a terminal sac.[3] Amyand has, therefore, two distinct claims to fame.

It is quite clear that in medical textbooks statements of alleged historical accuracy are copied without reference to originals. The much quoted case of Mestivier[4] is an example of inaccurate quotation and is of little importance in the history of appendicitis. Mestivier described a patient who developed a large abscess in the right side of the abdomen. The abscess was opened and much pus was evacuated. The patient died and at necropsy the caecum was found to have necrotic patches (*"parsemé d'escarres gangreneuses"*). The appendix contained a corroded pin, but there is no mention of the appearance of the organ, of inflammation, or of perforation. Mestivier suggests that the pin by irritation may have caused the illness (. . . *"que c'étoit-elle qui, irritant sans cesse les differentes tuniques qui entrent dans sa composition, y avoit determine tous les accidens de la maladie . . ."*). This case is frequently quoted as the first in which operation was performed for appendicitis, as the first account of appendicular inflammation, or as the first example of perforation due to a foreign body. If it is read in the original it is, as I translate it, merely an early account of a foreign body in the appendix.

It is surprising that the rediscovery of Claudius Amyand as the first appendicectomist should apparently have eluded the historians of St. George's Hospital and of British surgery. We must pay tribute to the scholarly research of Dr. Creese and thank him for bringing to light this most interesting and graphic item of surgical history.—I am, etc.,

Liverpool, 7. JOHN A. SHEPHERD.

REFERENCES

[1] *Surg. Gynec. Obstet.*, 1953, **97**, 643.
[2] *Philos. Trans.*, 1745, **43**, 369.
[3] Ibid., 1735, **39**, 329.
[4] *J. Med. Chir. Pharm.*, 1759, **10**, 441.

SIR,—Judgment, based on implication, is always tricky and often fallacious, as in Mr. Raymond Helsby's comments (*Journal*, December 26, 1953, p. 1434) on the details of a case of true strangulation of an appendix in a femoral sac which I gave in the *Journal* (November 28, 1953, p. 1216). The excision of the appendix from "below" was simply an *ad hoc* manœuvre to deal with the particular set of circumstances presenting—with the appendix and cone of caecum temptingly displayed. The implication drawn about the habitual use of this method was quite erroneous, as witness the fact that in over 12 years of operating under a wide variety of circumstances I have used the low approach only four times, including the case in question. Perhaps, however, Mr. Helsby's object in writing was primarily to use the letter as a medium for advocating McEvedy's approach, of which he is clearly a devotee. I, also, am familiar with and appreciative of its merits. However, in operating upon strangulated femoral herniae I almost invariably use a crease incision over the inguinal ligament, then, as a first step, dissect the sac out from below for several reasons: (1) It allows safe evacuation of the toxic, infective, and frequently haemorrhagic fluid present in the sac, instead of draining it to the peritoneum. (2) It allows clearing of oedematous and adherent fat from the sac, rendering its reduction easy and neat. (3) It allows inspection of the contents providing useful information before reduction. (4) It allows a combination of manipulations from below and above (as the next step is exposure of the canal from above by the usual route through the floor of the inguinal canal) giving greater control over safe reduction.

It was in making this preliminary inspection from below that I decided, on finding both canal and herniated organ small, just to complete the operation from this angle. I omitted these details from the description of the case, as I was mainly interested in describing the pathology, which was not the usual inflamed appendix in a hernial sac, but a genuine strangulation of a loop of the organ.—I am, etc.,

Wolverhampton. HENRY B. YOUNG.

Royal Medical Benevolent Fund Christmas Gifts

SIR,—It is a very great pleasure to report that the amount contributed to the Christmas Gifts Fund was most satisfactory and exceeded that of all previous years. It is impossible for me to thank the contributors personally for their generous response to my appeal, but through you, Sir, I should like to thank all your readers who have helped. I am especially grateful to the many B.M.A. Divisions and Branches, medical societies, and local medical committees who either forwarded donations from their own funds or arranged for collections to be made at an autumn meeting.

The many messages of good will sent with donations show how much this Christmas effort of the Royal Medical Benevolent Fund is approved of by the profession. It is hoped that as each Christmas comes round this work of kindness and good fellowship will be continued. I ask those who read the Christmas Appeals in future to bear in mind the intense pleasure and gratitude felt and expressed by those who benefit from the Appeal. I desire to express my own very sincere appreciation of the generosity which has been shown.—I am, etc.,

WEBB-JOHNSON,
London, S.W.15. President, Royal Medical Benevolent Fund.

Obituary

WILFRED SHAW, M.D., F.R.C.S., F.R.C.O.G.

Dr. J. B. GURNEY SMITH writes: Wilfred Shaw, whose obituary was printed in the *Journal* of December 19, 1953 (p. 1380), was certainly one of the many original personalities who have graced the honorary staff of Bart's. He had a very concise mind, which was readily reflected both in his clinical lectures and on his ward rounds, which always drew large numbers of students. In the theatre he was always bold and fearless, especially if the operation was of a dramatic order such as removal of a large ovarian cyst or a caesarean section. One of his most striking attributes was a wonderful sense of humour, and many of his pungent quips are as fresh to-day as when they were first uttered. Life was never slow when he was about. He was a notable successor to a long line of eminent Bart's physician accoucheurs, comprising Matthews Duncan, Sir Francis Champneys, Herbert Williamson, and my own very revered and beloved chief, John D. Barris. His going creates a gap which it will be difficult to fill, and all Bart's men who knew him will feel that they have lost a real friend.

G. A. S. H. writes: Probably because of his pungent wit, behind which lay his inherent kindliness, Wilfred Shaw proved himself a brilliant teacher to whom I turned repeatedly for fresh advice. Above all, he had that rare capacity for setting people at ease, and of encouraging their confidence within a few minutes—a fair tribute, I feel, to his character, as well as to his acknowledged supremacy in his own branch of medicine. I know that I was fortunate to be able to work under him.

Flying Officer A. L. C. DUNCAN was tragically killed on November 7, 1953, in a shooting incident at Buraimi in the Persian Gulf. He was a young man of exceptional promise in his profession and will be greatly missed. Alexander Leslie Cameron Duncan was born on June 6, 1928, and was educated at Jordanhill College School and at Glasgow University, where he graduated M.B., Ch.B. in January, 1952. In his student days he was a violinist in the university orchestra. After graduation he held house-surgeon and house-physician posts at Stonehouse Hospital, Lanarkshire, and Bridge of Earn Hospital, Perthshire, and was an outstandingly good resident. His capacity for work appeared unlimited, yet he could remain cheerful and unruffled under the most harassing conditions. He was kind and gentle towards his patients and their welfare was always his first consideration. He had intended to become a general practitioner, and with his enthusiasm for work and his qualities of sympathy and humanity he would undoubtedly have done a great deal of good in that role. In the Royal Air Force, which he entered last March for his period of National Service, he held several posts in the Canal Zone and latterly served with the Trucial Oman Services, setting up surgeries in the native villages and meeting and overcoming difficulties with his usual good humour and imperturbability. Although he was at Stonehouse Hospital for only six months, he is unlikely to be forgotten, and the deep sympathy of his ex-colleagues there is extended to his parents, brother, and sisters.—T. G. G.

The death of Dr. HUTCHISON BURT on December 1, 1953, at the age of 49 was a tragic loss to his family and to the specialty of psychiatry in the West Riding of Yorkshire, where he was medical superintendent of Stanley Royd Hospital, Wakefield, and consultant psychiatrist to the Leeds Regional Hospital Board. A Scotsman, Hutchison Burt was born on January 8, 1904, and was educated at Ayr Academy and at Glasgow University, where he won many class honours and graduated M.B., Ch.B. in 1926 with distinction in forensic medicine. After three and a half years of wide experience in general practice in Ayrshire he took up psychiatry as assistant medical officer at Glengall Hospital, under the late Dr. G. Douglas McRae. In 1933 he left Scotland for the industrial north of England to pursue his specialty at Wakefield Mental Hospital, where he worked until his untimely death, becoming senior assistant in 1938, deputy medical superintendent in 1947, and medical superintendent in 1949. He took the D.P.M. of Leeds University in 1934. One of his special interests was pathology, and he had published work on dysentery carriers.

The patients and staff of the hospital, the character of which he helped to shape, held him in high regard. He fostered the recreational interests of the nurses and was himself a notable cricketer in the hospital team. Since 1949 he had been honorary lecturer in psychiatry to Leeds University and was keenly interested in teaching. Shortly before his death he had begun to take an interest in the psychiatric training of the students at the School of Remedial Gymnasts at Pinderfields General Hospital. Because of the great dearth of psychiatric social workers, he, in collaboration with Professor C. Fraser Brockington, organized courses of study for unqualified mental health workers for the West Riding County Council. He was interested also in mental deficiency as a branch of psychological medicine, and many of those concerned with problems of mental defectives will miss his advice. In the region he worked assiduously to develop and extend the influence of the mental hospital into the community and helped to establish many out-patient clinics in the area as far apart as Doncaster, Leeds, and Pontefract. He never spared himself in the service of others, and although for many years in poor health he gave himself cheerfully to his patients. The peace of mind he must have brought to countless of the distressed is incalculable. He leaves a widow and two schoolboy sons.—P. F. F.

The death occurred on December 19, 1953, at his home near Sittingbourne, Kent, of Dr. S. W. INNES-SMITH at the age of 56. A member of an old Scottish family, Stuart William Innes-Smith was born at Sheffield on July 4, 1897, the elder son of the late Dr. R. W. Innes-Smith, whom he succeeded as surgeon to many of the great steelworks in Sheffield. He also carried on the works' ambulance movement originated by his father. Shortly after leaving Epsom he joined the Army and served as a combatant in the first world war, being awarded the Military Medal for gallantry in action. After the war he studied medicine at Edinburgh and Sheffield Universities and qualified M.R.C.S., L.R.C.P. in 1925. He then went into practice in Sheffield until, shortly before the last war, he emigrated to a remote part of Southern Rhodesia, where he was medical officer in an area the size of Wales. He performed many operations in a tiny clinic with only a native orderly to assist him, and he also did much dental and forensic work. During the last war he held a commission in the R.A.F., and in 1948 he returned to England. He was disillusioned to find that at the age of 52 it was difficult to obtain an appointment under the National Health Service, so he became a ship surgeon and in the course of his duties accompanied troops to Korea. Latterly he travelled to and from New Zealand. He was a kindly, generous, and sympathetic man and will be mourned by many of the poorer people of Sheffield, whom he helped during the period of depression before the last war, and by countless patients and friends both in this country and abroad. Despite a long and serious illness, during which he never complained, he did not give up work until three weeks before his death.

Medico-Legal

DEATH NOT DUE TO SWAB

[FROM OUR MEDICO-LEGAL CORRESPONDENT]

On October 8, 1953, Mrs. Mary Petty, a married woman 38 years old with four children, died in the Bradford Royal Infirmary. At the inquest held by the Bradford city coroner, Mr. R. S. Bishop, the verdict was recorded that the cause of death was general peritonitis due to multiple perforations of the large bowel due to ulcerative colitis (natural causes).

At necropsy a surgical swab 17½ by 11½ in. (45 by 30 cm.) was found. Dr. J. Eastwood, who performed the necropsy, thought at the time that the swab was inside the intestine, but Professor C. J. Polson, of the Department of Forensic Medicine of Leeds University, after consultation with Dr. Eastwood, came to the conclusion that it had probably been lying in the abdominal cavity beside the intestine and closely applied to it by fibrinous adhesions. The strong probability, he considered, was that the swab had been introduced during the delivery of Mrs. Petty's fourth child by caesarean section in March, 1953. He thought it most unlikely that such a swab could have entered through the mouth, and that, if it had, symptoms of digestive disturbance could not have been delayed until the third week of July, 1953, the first time they had become apparent. There was ulceration of the lower part of the large bowel at the recto-sigmoid junction well below the position in which the swab was found, and there were natural changes found capable of causing intestinal obstruction. Where the swab was found there was no sign of obstruction. There was also ulceration and perforation of the colon at the recto-sigmoid junction. Professor Polson concluded that the presence of the swab did not cause the disease from which Mrs. Petty died, and had no effect in accelerating her death.

Universities and Colleges

UNIVERSITY OF OXFORD

In Congregation on November 21 the degree of D.M. was conferred on P. B. S. Fowler.

The Welsh Memorial Drawing Prize in Anatomy has been awarded to Richard Charles Cook, scholar of Merton College.

UNIVERSITY OF CAMBRIDGE

Dr. G. A. Gresham has been appointed a University Demonstrator in Pathology with tenure from October 1, 1953, for three years.

UNIVERSITY OF LONDON

The following have been nominated, appointed, or reappointed as representatives of the University on the governing bodies of the institutions indicated in parentheses: Dr. J. F. Smith (Guy's Hospital Medical School); Sir Francis Fraser (Board of Management of the London School of Hygiene and Tropical Medicine); Professor A. A. Moncrieff, Professor J. Z. Young, F.R.S., and Mr. R. C. Davenport (Court of Governors of the London School of Hygiene and Tropical Medicine).

The following have been recognized as teachers of the University in the subjects indicated in parentheses: *St. Thomas's Hospital Medical School*, Dr. H. E. de Wardener (Medicine); *University College Hospital Medical School*, Dr. B. G. B. Lucas (Anaesthetics); *St. Mary's Hospital Medical School*, Dr. M. W. Ll. Owen (Anaesthetics).

Probationary recognition as teachers of the University in the subjects indicated in parentheses for two years from November, 1953, has been granted to the following: *University College Hospital Medical School*, Dr. W. B. Balderston (Dental Surgery); *St. Mary's Hospital Medical School*, Dr. R. H. Heptinstall (Pathology).

The following candidates have been approved at the examination indicated:

THIRD M.B., B.S.—[1 4]D. A. Alderson, [1 3 4]C. J. Edmonds, [1 3]C. J. Hayter, [1 3 4]P. J. Huntingford, [1 5]Gillian A. J. Lomax, [1 2]D. J. Parry, [1 4]A. C. Pollard, [1 2]V. M. Rosenoer, [1 4]F. T. Sai, [1 2]Gisela S. Seligmann, [1 5]Elizabeth J. Steele, M. E. N. Anfilogoff, P. D. Arnold, T. O. Atkinson, G. M. L. Baer, P. A. Barker, K. E. Barrett, Monica K. Barrett, A. A. Bartholomew, J. R. S. Barton, M. C. Batcheldor, M. C. Bate, B. S. Beardsworth, A. O. C. Beattie, P. J. Bell, Ruth Bell, E. D. L. Bennett, G. H. Bevan, J. A. Bevan, F. A. F. Biddle, D. L. J. Bilbey, F. Bilbey, C. E. S. Bill, A. O. Billinghurst, C. Bishop, R. C. Blake, P. O. Bodley, Evelyn A. M. Boesen, D. F. Boomla, J. L. Bourdillon, C. C. Bratt, M. Bray, D. W. Breese, R. G. Brenchley, O. V. Briscoe, Nancy G. Brockbank, J. R. Brook, R. C. Brookes, N. C. Brooks, J. R. Brown, Hilary E. S. Budd, J. Bullen, W. Bust, Pamela M. Butcher, J. E. Cairns, N. V. S. Calderon, J. D. Campling, J. L. H. Capper, Y. M. Chaiken, D. R. Chambers, F. A. Chandra, P. S. N. Chappell, B. Cheng, G. J. R. Clarke, H. J. Clarke, T. A. P. Clarke, A. Clark-Jones, H. J. W. Cleeve, W. E. Clifford-Jones, J. T. Coals, R. J. C. Cobbold, A. D. Cole, J. D. C. Cook, Barbara P. Coppen, R. McK. Corfield, J. Cottam, J. Crause, M. d'A. Crawfurd, D. J. Cripps, Elizabeth Cross, Margaret R. Cudkowicz, W. E. N. Cummings, Joan M. Curtis, P. Cushman, H. F. Davies, Margaret B. Davies, W. F. T. Davies, José A. Day, J. Dobbing, J. R. Duke, R. A. S. Dunn, B. J. MacD. Duxbury, K. Dyson, A. W. T. Eade, H. B. Edghill, Mary T. Edmonds, J. D'A. Edwards, D. R. Elam, W. J. Elder, Joan Endean, M. Evans, Frances M. Fisher, Gillian France, R. C. Francis, P. J. Frost, A. J. Fry, D. R. Gander, R. C. Giles, B. Gillespie, J. H. Goode, G. T. Goodey, Elizabeth B. Grantham, A. N. Green, F. V. Griffiths, M. V. Gruchy, R. Haggett, Mureen E. Hall, Dorothy J. Harden, Audrey Hardwick, D. Harris, R. W. Harris, W. C. Harris, J. A. Harrison, R. J. C. Hart, R. E. G. Harvey, Margaret A. Hatton, G. L. Haworth, Margaret M. Heley, M. D. Hickman, C. J. M. Hill, E. J. Hill, Rosemary A. Hill, P. O. Hirsch, C. F. Hoad, G. Y. P. Hobart, J. M. Hughes, A. G. Hughesdon, C. A. Hyde, R. K. Hyland, D. S. Iles, Eileen S. Jackson, H. G. Jenkins, Emily B. John, Anne F. Jones, J. J. Jones, R. F. N. Jones, A. R. Jordan, Sylvia J. Jordan, Brigid Keane, Sylvia J. Keet, D. B. Ker, M. Laurence, C. E. Lay, Pamela F. Lind-Smith, R. M. Liscombe, A. V. Livingstone, H. M. Lloyd, Robina S. Lock, D. B. Longmore, R. L. J. Lovick, Ann H. Low, J. A. Lunn, T. M. McAneny, R. M. A. McClelland, I. R. McDonald, J. G. Macdonald, W. M. McIsaac, Chloe Majolier, T. S. Mangat, H. St. J. Mansbridge, Patricia S. Matthew, Bridget d'E. Matthews, O. V. Maxim, Jean E. Moffat, R. O. Mohabir, J. B. Montgomery, R. J. Morgan, S. D. Morgan, J. C. Muir, Ann G. Mullins, T. N. Munro, A. P. Murphy, D. S. Nachshen, D. Naidoo, B. E. H. Neal, R. H. Neeve, C. G. Nicholson, Sheila Nourse, M. R. Oates, A. B. Oliveira, R. G. Orr, Patricia O'Sullivan, H. R. Owadally, R. B. Pardoe, J. V. Parson, J. D. W. Peck, P. R. Penty, J. P. Perry, J. H. Peters, Elizabeth M. Phillips, L. A. Phillips, A. F. W. M. Pooler, Caroline R. F. Port, L. J. Posener, April G. L. Powlett, J. W. H. Pretty, J. F. Pritchard, I. E. Purkis, Margaret J. Purser, I. F. S. Rae, H. J. Rayner, B. E. L. C. Reedy, M. T. Richards, Priscilla A. Ridge, A. H. M. Rimmer, Sheila M. Ritchie, A. A. Roe, J. A. Roopchand, F. E. N. Roper, J. R. Samuel, J. W. Scopes, H. G. Scott, Jean E. Sephton, Rita W. Shannon, D. E. Sharland, D. M. Shaw, F. E. Shaw, P. Shelmerdine, D. C. Shields, Jean M. Shields, J. D. Shone, W. S. Sinton, S. Sivasithamparam, D. A. D. Slattery, G. F. Slocombe, Marguerite L. Sloper, P. C. Smart, C. G. L. Smith, E. B. O. Smith, J. Southgate, Ethel M. Spencer, G. R. Stevenson, A. P. O. Stewart, T. F. Stoyle, R. J. Sturt, F. L. H. Sugden, R. L. G. Sutcliffe, N. D. V. Swallow, A. P. Tannen, W. H. H. Taylor, E. M. Thomas, G. E. Thomas, R. V. Ll. Thomas, S. G. Thompson, A. D. Tuddenham, F. B. Valentine-Hagart, Heather F. A. Vickery, R. MacD. Vining, T. Wade West, D. J. Waller, H. W. C. Ward, D. Wardale, I. C. Ware, A. M. Warrington, S. A. Watkins, D. S. Watson, H. P. Watson, R. Watts, E. L. Webb, G. F. K. Webb, J. W. S. Webb, Jean M. Weddell, Dorothy A. Westcott, J. A. Whillis, C. J. White, Dorothy J. Whitney, J. R. Wilde, D. Wilkinson, C. A. Williams, J. L. Wilson, A. S. Wint, Edna D. C. S. Wood, J. G. Wotherspoon, C. E. Wright, R. W. P. Yates, T. G. Young, W. O. C. Young.

[1]With honours. [2]Distinguished in pathology. [3]Distinguished in medicine. [4]Distinguished in applied pharmacology and therapeutics. [5]Distinguished in surgery. [6]Distinguished in obstetrics and gynaecology.

UNIVERSITY OF BIRMINGHAM

Dr. J. A. H. Waterhouse, Lecturer in Human Genetics, has been given the title of Reader in Medical Statistics.

Dr. P. L. Krohn has resigned his Readership in Endocrinology in order to accept a Nuffield Gerontological Research Fellowship, to date from October 1, 1953, in the Department of Anatomy.

Dr. W. D. Carruthers has provided funds to establish an annual prize in social medicine to the value of five guineas. The prize

is in memory of the late Dr. Bostock Hill, professor of hygiene and public health from 1893 to 1919.

The following appointments are announced: Dr. Douglas B. Brewer, Senior Lecturer in Pathology, Dr. R. Lannigan, Lecturer in Pathology, and Dr. E. A. Smith, Research Fellow in Social Medicine, all from October 1, 1953; Dr. E. J. Hamley, Lecturer in Physiology from December 1, 1953; Dr. E. A. Cooper, University Research Fellow in the Department of Medicine from October 16, 1953.

Dr. P. B. Marshall, Lecturer in Pharmacology, Dr. J. L. Stafford, Lecturer in Pathology, and Dr. K. White, Lecturer in Physiology, have resigned their appointments.

UNIVERSITY OF SHEFFIELD

The following appointments are announced: Dr. T. J. Rendle-Short, Full-time Lecturer in Child Health; Dr. K. S. Holt, Full-time Tutor in Child Health; and Dr. D. H. Anderson, Part-time Clinical Teacher in Chest Diseases.

Dr. Irving Gordon, of the New York State Department of Health, has been appointed Visiting Senior Lecturer in Bacteriology during his visit to the University during the present session.

Dr. J. Mackinnon has resigned his appointment as Research Assistant in the Department of Medicine.

At a degree Congregation held on December 15, 1953, the following degrees were conferred:

M.B., CH.B.—S. H. Harrison, T. G. Kershaw, G. F. Mackenzie, G. F. C. Rosser, P. Sykes, Helen F. Taylor, P. Taylor, D. W. Warrell, Cynthia M. Worrall.

QUEEN'S UNIVERSITY, BELFAST

Dr. R. A. Womersley, M.R.C.P., has been appointed to a lectureship in medicine in the University.

ROYAL COLLEGE OF SURGEONS OF ENGLAND

At a meeting of the Council of the College held on November 12, with Sir Reginald Watson-Jones, Vice-President, in the chair, Professor Lambert Rogers was appointed as the Bradshaw Lecturer and Professor F. Wood Jones as the Thomas Vicary Lecturer for 1954.

The death of Mr. R. H. Burne (Hunterian Trustee and past Physiological Curator) was reported and the Council unanimously adopted a resolution of condolence.

Professor F. C. Wilkinson was co-opted as the Member of the Council representing Dental Surgery in place of Sir William Kelsey Fry.

The Begley Prize was awarded to Margaret M. Heley (Royal Free).

Licences to practise were conferred upon the successful candidates whose names were printed in the report of the meeting of the Royal College of Physicians of London (*Journal*, December 26, 1953, p. 1437) and to I. P. Vaughan.

Diplomas were granted, jointly with the Royal College of Physicians of London, in Medical Radio-Diagnosis, in Medical Radiotherapy, in Child Health, and in Ophthalmology, to the successful candidates whose names were printed in the report of the meeting of the Royal College of Physicians of London (*Journal*, December 26, 1953, p. 1437).

ROYAL FACULTY OF PHYSICIANS AND SURGEONS OF GLASGOW

At a meeting of the Faculty held on December 7, 1953, with the President, Dr. Andrew Allison, in the chair, the following were admitted Fellows of Faculty: *qua Physician*, Saw Mra Aung, H. W. Boyd, T. Cochrane, A. F. Toboku-Metzger; *qua Surgeon*, J. P. Fraser, S. R. Ganeshiya.

ROYAL COLLEGE OF SURGEONS IN IRELAND

On November 20 the Fellowship of the College was conferred on E. G. Leahy and A. McCalister.

ROYAL MEDICO-PSYCHOLOGICAL ASSOCIATION

The following candidates were successful at the November examination for the Diploma in Psychological Medicine:

D.P.M.—*Part I:* M. J. Raymond, H. K. Rose, G. S. Stirling. *Part II:* J. D. C. Currie, R. S. Ferguson, T. E. Hall, I. E. J. McLauchlan, M. J. Raymond, A. Smellie, Elizabeth Shoenberg.

ROYAL AUSTRALASIAN COLLEGE OF PHYSICIANS

The following, having satisfied the Board of Censors in Australia, were admitted to the Membership of the College in October, 1953: J. Benecke, G. L. Bennett, J. W. Bennett, R. B. Blacket, W. H. Cary, G. W. Cooper, D. L. Hobson, K. S. Millingen, N. M. Newman, R. F. O'Shea, J. G. Richards, P. M. Robertson, L. C. A. Watson.

INFECTIOUS DISEASES AND VITAL STATISTICS

Summary for British Isles for week ending **December 19** (No. 50) and corresponding week 1952.

Figures of *cases* are for the countries shown and London administrative county. Figures of *deaths* and *births* are for the 160 great towns in England and Wales (London included), London administrative county, the 17 principal towns in Scotland, the 10 principal towns in Northern Ireland and the 14 principal towns in Eire.

A blank space denotes disease not notifiable or no return available.

The table is based on information supplied by the Registrars-General of England and Wales, Scotland, N. Ireland, and Eire, the Ministry of Health and Local Government of N. Ireland, and the Department of Health of Eire

CASES in Countries and London	1953					1952				
	Eng. & Wales	Lond.	Scot.	N. Ire.	Eire	Eng. & Wales	Lond.	Scot.	N. Ire.	Eire
Diphtheria	16	1	5	0	2	23	3	7	1	1
Dysentery	503	95	156	3	1	328	10	75	2	2
Encephalitis, acute	3	0	0	0		10	1	0	0	
Enteric fever:										
Typhoid	1	0	1	0		1	0	1	0	6
Paratyphoid	4	0	0	0		4	1	2 (B)	0	0
Food-poisoning	141	10		0		74	11		1	
Infective enteritis or diarrhoea under 2 years				14	14				13	13
Measles*	778	12	42	16	66	17,742	1404	241	27	113
Meningococcal infection	22	1	13	1	2	39	4	13	2	2
Ophthalmia neonatorum	30	2	6	0		32	1	7	0	
Pneumonia†	692	43	242	12		1,135	131	472	8	1
Poliomyelitis, acute:										
Paralytic	39	2	8	3	7	41	1	2	3	2
Non-paralytic	12	1				17	2			
Puerperal fever§	259	47	10	0		233	35	16	1	1
Scarlet fever	1,284	61	202	30	46	2,229	131	302	34	70
Tuberculosis:										
Respiratory			142	22				133	22	
Non-respiratory			24	4				24	5	
Whooping-cough	2,304	101	396	60	32	1,865	75	129	21	122

DEATHS in Great Towns	1953					1952				
	Eng. & Wales	Lond.	Scot.	N. Ire.	Eire	Eng. & Wales	Lond.	Scot.	N. Ire.	Eire
Diphtheria	0	0	0	0	0	1	0	0	0	0
Dysentery	0	0		0		1	0		0	
Encephalitis, acute		1			0		0			0
Enteric fever	0	0	0	0		0	0	0	0	
Infective enteritis or diarrhoea under 2 years	7	1	0	1	1	10	2	3	1	0
Influenza	17	3	3	1	0	60	24	4	1	1
Measles		0	0	1	0		0	0	0	0
Meningococcal infection		0	1				1	2		
Pneumonia	226	28	21	10	6	597	168		8	16
Poliomyelitis, acute	6	1			0	4	1			0
Scarlet fever		0	0	0	0		0	0	0	0
Tuberculosis:										
Respiratory	88	14	17	6	6	259	77	31	3	7
Non-respiratory		1	1	0	0		5	1	0	2
Whooping-cough	2	0	0	0	0	6	0	0	0	0
Deaths 0–1 year	217	20	25	10	21	295	54	49	18	18
Deaths (excluding stillbirths)	5,072	725	559	106	184	9,452	2484	861	143	224
LIVE BIRTHS	6,680	996	783	212	352	7,157	1050	854	211	342
STILLBIRTHS	199	25	19			202	22	26		

* Measles not notifiable in Scotland, whence returns are approximate.
† Includes primary and influenzal pneumonia.
§ Includes puerperal pyrexia.

Vital Statistics

England and Wales in 1952

Of the Regions and large conurbations Greater London had the lowest death rate in 1952 (10 per 1.000 population), in spite of its December fog, and the West Midlands conurbation (including Birmingham) came next with a rate of 10.2. At the other end of the scale were the West Yorkshire conurbation (including Leeds and Bradford) with a rate of 13.1, and North Wales with a rate of 12.8. The rate for the whole of England and Wales was 11.3. For infant mortality Greater London again had the lowest figure (22 deaths per 1,000 live births), while the Merseyside conurbation had the highest figure (35) followed by South Wales (34). The rate for the whole of England and Wales was 28.

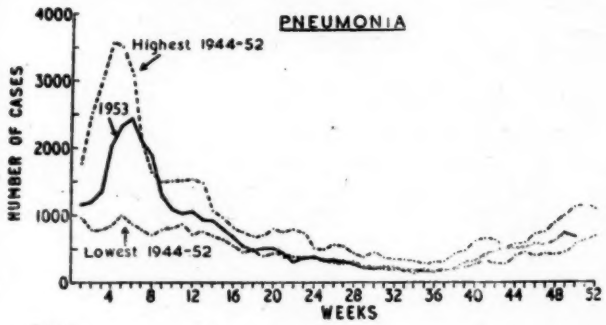
These figures are from the Registrar-General's *Statistical Review for the Year 1952, Tables, Part 1, Medical* (H.M.S.O., 10s.), the first review for many years to appear within a year of the period to which it relates.

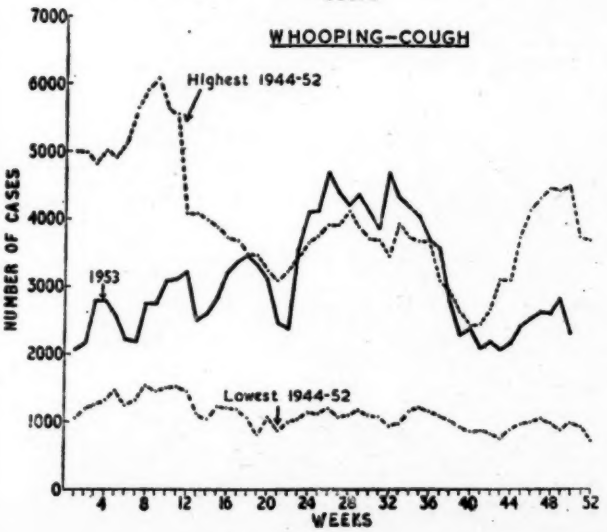
Week Ending December 26

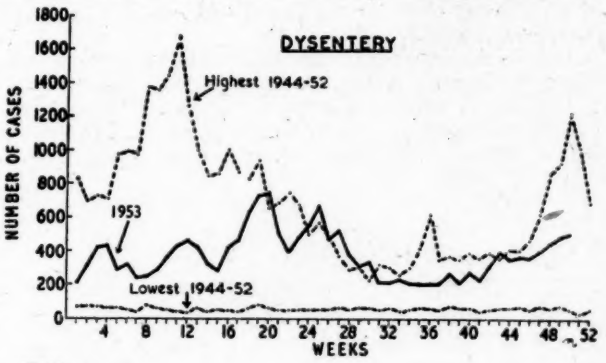
The notifications of infectious diseases in England and Wales during the week included scarlet fever 949, whooping-cough 1,424, diphtheria 15, measles 611, dysentery 309, acute poliomyelitis 29, paratyphoid fever 1, and typhoid fever 0.

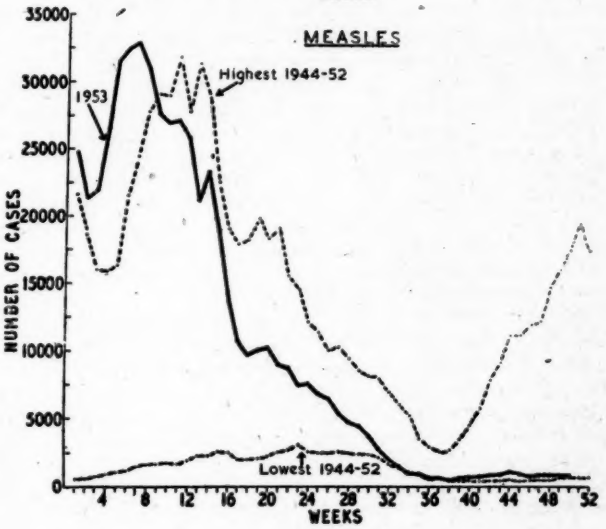
Graphs of Infectious Diseases

The graphs below show the uncorrected numbers of cases of certain diseases notified weekly in England and Wales. Highest and lowest figures reported in each week during the nine years 1944–52 are shown thus - - - - - - -, the figures for 1953 thus ———. Except for the curves showing notifications in 1953, the graphs were prepared at the Department of Medical Statistics and Epidemiology, London School of Hygiene and Tropical Medicine.









Infectious Diseases

Infectious diseases were less prevalent in England and Wales during the week ending December 19. The falls in the number of notifications were 452 for whooping-cough, from 2,756 to 2,304, 162 for scarlet fever, from 1,446 to 1,284, and 105 for measles, from 883 to 778.

The largest declines in the incidence of whooping-cough were 113 in Lancashire, from 333 to 220, 53 in Glamorganshire, from 136 to 83, 44 in Staffordshire, from 138 to 94, and 35 in Norfolk, from 79 to 44. The only large fall in the local trends of scarlet fever was 52 in Lancashire, from 242 to 190. 16 cases of diphtheria were notified, being 5 fewer than in the preceding week. The chief features of the returns of diphtheria were falls in Staffordshire from 7 to 4 and in Lancashire from 4 to 1, and a rise in Durham from 2 to 5. The only fluctuations in the trends of measles of any size were falls of 37 in Staffordshire, from 119 to 82, and 30 in Cumberland, from 87 to 57.

51 cases of acute poliomyelitis were notified during the week. These were 7 fewer for paralytic and 1 fewer for non-paralytic cases than in the preceding week. The largest returns were Lancashire 8, Wiltshire 4, and Middlesex 4.

In contrast to the other infectious diseases the number of notifications of dysentery increased by 18, from 485 to 503. The largest centres of infection were London 95 (Islington 21, Lewisham 10, Wandsworth 9), Lancashire 71 (Bolton C.B. 31, Manchester C.B. 16), Yorkshire West Riding 47 (Bradford C.B. 24, Shipley U.D. 9), Surrey 39 (Egham U.D. 18, Frimley and Camberley U.D. 18), Essex 30 (Barking M.B. 17), Durham 30 (Lanchester R.D. 23), Norfolk 27 (Norwich C.B. 27), Leicestershire 25 (Leicester C.B. 23), and Middlesex 20.

Industrial Accidents and Diseases

The number of workpeople (other than seamen) in the United Kingdom whose deaths from accidents in the course of their employment were reported in November, 1953, was

124, compared with 124 in the previous month and 129 in November, 1952.

The number of cases of industrial diseases in the United Kingdom reported during November was as follows: lead poisoning, 4; other poisoning, 0; anthrax, 7; epitheliomatous ulceration, 8; and chrome ulceration, 15; total, 34. There were no deaths.—*Ministry of Labour Gazette*, December, 1953.

Medical News

Cataract and Glaucoma.—Professor Arnold Sorsby's report on "The Causes of Blindness in England, 1948–50" (H.M.S.O., 1953) and his more recent analysis in the Ministry of Health's report for 1952 have made it abundantly clear what a high place cataract and glaucoma now occupy in causing blindness in this country. In round figures 3,000 persons were placed on the Blind Register during the year 1951–2 because of cataract and 1,500 because of glaucoma. These two conditions account for over 40% of the new registrations in England and Wales. What is less well known and far more disturbing is that probably much of this blindness could have been prevented. According to a recent Ministry of Health circular to regional hospital boards and management committees, asking for an urgent review of the arrangements for the treatment of such cases, four out of every five patients with cataract placed on the Register in 1951–2 had received no treatment. At the lowest estimate, the circular puts the number of these "whose sight might well have been saved by surgical treatment" at 1,000. One reason for this state of affairs may have been the long waiting-list for ophthalmic beds. Although between 1950 and 1952 the number of ophthalmic hospital beds in England and Wales had risen from 3,975 to 4,391, the waiting-list during that time jumped from 6,000 to 31,000. With glaucomatous patients early diagnosis is recognized as being the prime need. To facilitate this the circular suggests the establishment of special glaucoma clinics in ophthalmological departments.

Fellowships in Clinical Research.—The Medical Research Council is inviting applications for a further series of Fellowships in Clinical Research, tenable at centres in the United Kingdom during the academic year 1954–5. These Fellowships are open to suitably qualified medical graduates who desire to prepare themselves for a career in clinical research. It is intended that each Fellow appointed under the scheme should be given an opportunity to study methods of research in the basic subject most relevant to his particular clinical interest. The awards will be made for a period of one year in the first instance and will be renewable annually in approved cases up to a maximum of three years in all. Stipend will be at the rate of £850 per annum, rising by annual increments of £75 to £1,000 per annum, with superannuation provision in addition. Candidates for these Fellowships, which are ordinarily restricted to British subjects resident in the United Kingdom, must be medically qualified and clinically experienced, and should preferably have worked for a period in a department in which clinical research was in progress. Applicants will be invited to submit their own proposals as to type and place of work, but the Council will be glad to advise successful candidates on the selection of suitable centres of study and to assist in placing them in departments or laboratories where the desired training and experience can be obtained. Applications must be sponsored in each case by the head of the appropriate department in the candidate's university or medical school, and an undertaking will be required that a suitable academic post in a clinical department will be available to the candidate in that institution on satisfactory completion of the period of study under the Fellowship. Forms of application for these Fellowships may be obtained from the secretary, Medical Research Council, 38, Old Queen Street, London, S.W.1, with whom applications should be lodged as soon as possible, and in any event not later than March 1.

Viomycin.—A limited supply of viomycin, a new antibiotic with properties similar to streptomycin, will shortly be available to N.H.S. hospitals through the usual antibiotic distribution centres. Viomycin was developed in the United States. Its main indication is for cases of tuberculosis where the bacilli are found to be drug-resistant or where the patient is intolerant of conventional chemotherapy. It is contraindicated if there is impairment of renal function or non-tuberculous renal disease. Like other drugs used in the treatment of tuberculosis, viomycin quite commonly provokes toxic reactions, though generally these are transient and reversible.

Dalby Memorial Prize.—On the recommendation of the Council of the Section of Otology of the Royal Society of Medicine, the Society's Dalby Memorial Prize has been awarded to Mr. Terence E. Cawthorne for the best original work in otology during the previous five years.

Nuffield Dental Fellowships.—Details of the Nuffield Foundation's dental fellowships and scholarships are given in our advertisement pages this week at p. 49. One of the purposes of these fellowships is to enable selected graduates in medicine and science to receive training that will qualify them to undertake teaching and fundamental research on dental health and disease.

The "Half-Minute" Thermometer.—The British Standards Institution has rung the knell of the half-minute and the one-minute clinical thermometers. Because of the errors that may follow blind reliance on such timing instructions, a new Standard has been issued. Clinical thermometers will in future be marked "quick," "medium," or "stubby."

Sierra Leone Mission Hospital.—A gift of £40,000 by the former Lord Mayor of Newcastle, Alderman J. G. Nixon, to the Methodist Missionary Society has made possible the rebuilding of a 100-bedded mission hospital at Segbwema, Sierra Leone. Alderman Nixon recently went to West Africa to open the hospital.

COMING EVENTS

Mount Everest.—Mr. R. C. Evans and Dr. M. Ward will deliver a Hunterian Lecture on "The Ascent of Mount Everest: Medical Studies," on Wednesday, January 13, at 5.30 p.m., at the Royal College of Surgeons, Lincoln's Inn Fields, London, W.C.2.

NEW ISSUES

Abstracts of World Medicine.—The January issue (Vol. 15, No. 1), which is now available, contains abstracts of important papers on both medical and surgical subjects drawn from journals published in some 20 different countries and in all five continents. In addition to the various branches of clinical medicine and surgery, the subjects covered include pathology, bacteriology, pharmacology, and chemotherapy, and there are also sections dealing with medical genetics, public health, industrial medicine, anaesthetics, radiology, and the history of medicine.

Issued monthly; annual subscription £4 4s., single copy 8s. 6d.; a specimen will be sent free on request.

SOCIETIES AND LECTURES

A fee is charged or a ticket is required for attending lectures marked ●. Applications should be made first to the institution concerned.

Monday, January 11

INSTITUTE OF PSYCHIATRY.—5.30 p.m., lecture demonstration by Dr. E. Stengel.

MEDICAL SOCIETY OF LONDON.—8.30 p.m., discussion: Physical Basis of Mental Illness, to be introduced by Dr. R. A. J. Asher and Dr. T. A. H. Munro.

ROYAL COLLEGE OF PHYSICIANS OF LONDON.—5 p.m., Watson Smith Lecture by Dr. J. T. Ingram: Significance and Management of Psoriasis.

ROYAL EYE HOSPITAL.—5.15 p.m., Dr. T. H. Whittington: The Hypermetropic Patient. Astigmatism. Bifocals.

Tuesday, January 12

CHELSEA CLINICAL SOCIETY.—At South Kensington Hotel, 7.30 p.m., dinner, followed by a discussion on Sleep, to be opened by Sir Francis Walshe, F.R.S., and Dr. Denis Williams.

ILFORD MEDICAL SOCIETY.—At King George Hospital, Ilford, 8.45 p.m., film: A Two Year Old Goes to Hospital. Discussion to be opened by Dr. H. M. S. Davidson.

INSTITUTE OF DERMATOLOGY.—5.30 p.m., Dr. R. G. Cochrane: Leprosy.

ST. MARY'S HOSPITAL MEDICAL SCHOOL.—5 p.m., Professor Dugald Baird: Impact of Social Conditions on Labour.

Wednesday, January 13

INSTITUTE OF DERMATOLOGY.—5.30 p.m., Dr. R. W. Riddell: Histopathology of Fungous Infections.

MIDLAND MEDICAL SOCIETY.—At Selly Oak Hospital, Birmingham, 8.15 p.m., clinical meeting.

ROYAL COLLEGE OF SURGEONS OF ENGLAND.—5.30 p.m., Hunterian Lecture by Mr. R. Charles Evans and Dr. Michael Ward: The Ascent of Mount Everest: Medical Studies.

ROYAL EYE HOSPITAL.—5.30 p.m., Mr. L. H. Savin: Ophthalmic Operations and their Indications (3).

ROYAL FACULTY OF PHYSICIANS AND SURGEONS OF GLASGOW.—5 p.m., Finlayson Memorial Lecture by Professor L. J. Witts: Anaemia and the Alimentary Tract.

ST. MARY'S HOSPITAL MEDICAL SCHOOL.—5 p.m., Dr. D. F. O'Neill: Lecture-demonstration in Psychiatry.

SOCIETY FOR APPLIED BACTERIOLOGY.—At Institution of Civil Engineers, 10 a.m., business meeting. 2.15 p.m., joint meeting with Microbiology Group of Society of Chemical Industry. Symposium: Industrial Methods of Sterilization. Papers by Dr. M. Ingram, Mr. Osman Jones, Dr. R. Maxwell Savage, and Mr. G. Sykes.

Thursday, January 14

ALFRED ADLER MEDICAL SOCIETY.—At 11, Chandos Street, W., 8 p.m., Mr. R. W. Raven: Psychological Reaction to Surgical Disease.

BRITISH INSTITUTE OF RADIOLOGY.—8 p.m., Dr. J. Blair Hartley: Significance of Placental Calcification.

BRITISH POSTGRADUATE MEDICAL FEDERATION.—At London School of Hygiene and Tropical Medicine, 5.30 p.m., Dr. E. A. Carmichael: Hemispherectomy and Localization of Function.

●INSTITUTE OF CHILD HEALTH.—5.30 p.m., Dr. H. N. Davy: Behaviour in Epilepsy.

INSTITUTE OF LARYNGOLOGY AND OTOLOGY.—5 p.m., Professor F. C. Ormerod: Use of Antibiotics and Chemotherapy.

●LIVERPOOL MEDICAL INSTITUTION.—3 p.m. and 8 p.m., Mr. Charles Evans: Everest, 1953.

LONDON UNIVERSITY.—At Middlesex Hospital Medical School, 5 p.m., special university lecture in Human Anatomy and Morphology by Professor J. Pasteels (Brussels): Present Views on Embryonal Induction.

ROYAL ARMY MEDICAL COLLEGE.—5 p.m., Dr. W. C. Cockburn: Early Field Investigations of Typhoid Vaccines.

ROYAL COLLEGE OF SURGEONS OF ENGLAND.—5 p.m., Hunterian Lecture by Professor R. Milnes Walker: Place of Venous Shunts in the Treatment of Portal Hypertension.

ST. ANDREWS UNIVERSITY.—At Physiology Department, Dundee, 5 p.m., Professor L. J. Witts: Anaemia and the Alimentary Tract.

ST. GEORGE'S HOSPITAL MEDICAL SCHOOL.—5 p.m., neurology demonstration by Dr. J. H. Paterson.

SURREY INTER-HOSPITAL PSYCHIATRIC ASSOCIATION.—At West Park Hospital, Epsom, 7.30 p.m., clinical meeting. Papers by Dr. J. Zelmanowits, Mr. M. Klein, Dr. O. F. Garai, and Dr. M. K. Beattie.

UNIVERSITY COLLEGE LONDON: DEPARTMENT OF BIOCHEMISTRY.—Physiology Theatre, 4.45 p.m., Public Lecture by Professor Jean Brachet (Brussels): Role of Ribonucleic Acid in Morphogenesis.

Friday, January 15

BRITISH INSTITUTE OF RADIOLOGY.—5 p.m., meeting of medical members.

FACULTY OF RADIOLOGISTS.—At Royal College of Surgeons of England, 2.15 p.m., Radiodiagnosis Section Meeting. Dr. P. G. Keates: Physical, Physiological, and Hormonal Aspects of Hydronephrosis; Dr. C. J. Don: Bronchography in Pulmonary Tuberculosis.

INSTITUTE OF DERMATOLOGY.—5.30 p.m., clinical demonstration by Dr. R. G. Cochrane: Leprosy.

OSLER CLUB OF LONDON.—At 11, Chandos Street, W., 7.45 p.m., Professor J. M. R. Cormack, M.A.: Black Magic (in honour of Sir James Frazer, January 1, 1854-1941). Discussion: Professor Raymond Firth, H.E. Mme. Subandrio, and Dr. Michael S. M. Fordham.

POSTGRADUATE MEDICAL SCHOOL OF LONDON.—2 p.m., Professor R. Milnes Walker: Lesions of the Small Intestine.

ROYAL EYE HOSPITAL.—5 p.m., Miss M. Savory: Differential Diagnosis of Corneal Lesions.

ROYAL MEDICAL SOCIETY, Edinburgh.—8 p.m., Dissertation by Mr. K. Chapman: Toxaemia of Pregnancy.

UNIVERSITY COLLEGE LONDON: DEPARTMENT OF PHARMACOLOGY.—At Physiology Theatre, 5.30 p.m., Public Lecture by Professor Werner Koll (Göttingen): Experimental Studies on Analgesics—Tooth Stimulation and Other Methods.

Saturday, January 16

BIOCHEMICAL SOCIETY.—At Department of Chemical Pathology, Postgraduate Medical School of London, 11 a.m., 325th meeting. Scientific papers.

SOUTH-EAST METROPOLITAN REGIONAL TUBERCULOSIS SOCIETY.—At Farnborough Hospital, Kent, 10.30 for 11 a.m., extraordinary general meeting. Dr. D. G. Madigan will speak on his experiences in America.

BIRTHS, MARRIAGES, AND DEATHS

BIRTHS

Batten.—On November 26, 1953, at Queen Charlotte's Hospital, London, W., to Mary, wife of Henry Batten, M.B., F.R.C.S., a daughter—Jane.

Du Heaume.—On December 30, 1953, at Enfield, Middlesex, to May (formerly Giffin), wife of Brian du Heaume, M.B., B.S., D.Obst.R.C.O.G., a daughter—Susan.

Lewes.—On December 29, 1953, at Bedford General Hospital, to Daphne (formerly Wailes), wife of David Lewes, D.M., M.R.C.P., a fourth daughter—Christina.

McLaren.—On December 19, 1953, to Patricia Annette, wife of William J. McLaren, F.R.C.S., of Tranquille, British Columbia, Canada, a third son—Niall Fullerton.

Vowles.—On December 16, 1953, at the Royal Infirmary, Cardiff, to Mary (formerly Knowles), M.B., Ch.B., D.C.H., and Keith D. J. Vowles, M.B., F.R.C.S., a brother for Robert—Andrew John.

Woodall.—On December 17, 1953, to Jenifer, wife of John Woodall, M.B., B.S., of The Lodge, Cray Hall, North Cray, Kent, a son—Christopher John.

DEATHS

Douglas.—On December 10, 1953, at his home, 38, Prestbury Road, Cheltenham, Glos, Kenneth Harington Douglas, M.R.C.S., L.R.C.P., formerly of 41, Prospect Hill, London, E., aged 80.

Ewen.—On December 15, 1953, Gerald Anglin Ewen, M.R.C.S., L.R.C.P., of Ryde House, Twickenham, Middlesex, aged 43.

Schaefer.—On December 14, 1953, in a nursing home, London, Hans H. Schaefer, L.R.C.P.&S.Ed., L.R.F.P.S., of 251, Hertford Road, Enfield Highway, Middlesex.

Any Questions?

Correspondents should give their names and addresses (not for publication) and include all relevant details in their questions, which should be typed. We publish here a selection of those questions and answers which seem to be of general interest.

Coronary Disease and Dental Analgesics

Q.—*Are local analgesics for dental operations contra-indicated in those with coronary artery disease? Are any special precautions advised in such cases?*

A.—There is no reason why the average patient with coronary artery disease should not have a local analgesic of this sort. Where there is a history of a recent heart attack it is perhaps better to avoid the adrenaline. In any case the concentration of adrenaline in the solution should not exceed 1 in 200,000. Solutions commonly supplied for dental use often have a higher concentration of adrenaline than this.

Blood Pyruvates

Q.—*What is the value of a blood pyruvate estimation? What conclusions can be drawn if the level is raised, particularly in relation to peripheral neuritis?*

A.—Pyruvic acid is formed as an intermediary in the oxidation of glucose by the tissues. Vitamin B_1 (thiamine) is required for its further oxidation, and if this vitamin is not available in adequate amounts pyruvate accumulates in the blood. The estimation of blood pyruvate levels is therefore of interest as a means of assisting in the diagnosis of vitamin B_1 deficiency states. In the more chronic and less severe forms of thiamine deficiency the fasting blood pyruvate level is usually within the normal range; raised levels can, however, be demonstrated in many such patients if a "loading" dose of glucose is first given.

It must be realized also that conditions other than a deficiency of this vitamin can also cause impaired pyruvate oxidation with a resulting rise in the blood pyruvate level. In a patient with peripheral neuritis a raised level cannot by itself therefore be taken to indicate thiamine deficiency, although it would support this diagnosis. If, however, parenteral treatment with thiamine for, say, two weeks results in a return to normal of a previously elevated level, it would seem likely that a deficiency of this vitamin had existed. As the clinical response of such patients is often slow, blood pyruvate estimations before and after thiamine therapy can often provide a more rapid and surer indication of response to this therapy.

Malaria Prophylaxis

Q.—*What is the best malaria prophylactic for a European family visiting a malarious area? Please give details of dosage and frequency of administration, including any variations of these for infants and children. Are mosquito nets necessary if chemoprophylaxis is thorough?*

A.—Proguanil is probably the best antimalarial for a European family visiting a malarious area. The drug is prepared in tablets containing 100 mg. or 25 mg. Where proguanil-resistant strains of *P. falciparum* have been demonstrated, chloroquine should be taken instead.

The dosage of proguanil for adults is 100 mg. daily. Exceptionally—for example, in a big individual—twice this dose may be needed. For children, the dosage from birth to the second birthday is 25 mg. daily, and from the second to fifth birthday 50 to 100 mg. daily. Prophylaxis should begin a fortnight before entering the malarious area and continue for one month after leaving the area.

Most people find it easier to form the habit of taking a drug daily than once or twice a week. If, however, the latter is desired, chloroquine is advised. The drug is usually

prepared in tablets containing 250 mg. of the diphosphate. The dosage of chloroquine diphosphate for adults is 500 mg. once weekly. For children: from birth to the third birthday, 62.5 mg. once weekly; from the third to the sixth birthday, 125 mg.; over 6 years, 250 mg.; and over 10 years, the adult dose.

Alternative antimalarials are mepacrine and pyrimethamine ("daraprim"). The adult dose of mepacrine is 100 mg. daily, started a fortnight before entering the malarious area and continued for a month afterwards. Mepacrine is not as convenient as proguanil for children. Birth to second birthday: total dosage of 50 to 75 mg. in divided daily doses. From second to sixth birthday: total weekly dosage of 100 to 200 mg. in divided daily doses. From sixth to tenth birthday: total weekly dosage of 200 to 300 mg. in divided daily doses. From tenth to fifteenth birthday: total weekly dosage of 300 to 400 mg. in divided daily doses. Over 15 years, adult dose. The adult dose of pyrimethamine is 25 mg. once weekly. Half this dose has been found successful in children.

All drugs should be taken at some meal during the day with a good draught of fluid. Absorption is not affected by moderate quantities of alcohol. After cessation of suppressive therapy with any of the above drugs attacks of falciparum malaria should not develop. Vivax malaria may, however, appear and require radical therapy.

Some form of mechanical protection against insects is always desirable, even when drug suppression is successful. There are many insect-borne diseases other than malaria.

Artificial Materials for Hernia Repair

Q.—*What are the advantages and disadvantages of using materials such as nylon or wire for the repair of large hernias in place of fascia lata?*

A.—Those surgeons who use nylon and wire for the repair of large hernias regard the ready availability of the materials as a chief advantage. It is, however, doubtful whether a lattice or filigree of any foreign material is really as effective as a barrier of the patient's own tissues. The questioner refers to the use of fascia lata, a method introduced by the late W. E. Gallie and satisfactory in his hands. Those surgeons who object to his method have two main criticisms: first, the extra time taken in removing the fascial strip and the added risks of sepsis; and, secondly, the tendency for the inguinal ligament to be damaged by the large fascial needle, especially in patients with friable tissues. An effective barrier of the patient's own tissues can, in most cases of inguinal hernia, be provided by a rectus sheath slide operation, and many believe that this offers the advantages of a fascial repair with none of its disadvantages.

Lattices of nylon and wire all tend to fragment after a variable period of time. If the lattice is made very close critics of the method will point to the tendency for the inguinal ligament to be frayed by frequent passage of the needle. On the other hand, if the lattice is of a wide mesh, the tissues can readily bulge through the suture material. The tendency for nylon knots to slip can be irritating, and this objection is not entirely rectified by the use of braided nylon. Stainless steel wire tends to become fragmented by movement and electrolysis in the tissues, and is less in vogue than it was a few years ago. Tantalum similarly fragments on movement. Filigrees of tantalum or stainless steel also break up and tend to separate from their attachments; recurrences are therefore sometimes seen at the edge of a filigree. Silver wire is rarely used to-day: it is subject to all the objections already mentioned, with the additional one of occasionally staining the overlying skin black owing to the deposition of silver sulphide. There is some evidence to suggest that wire filigrees are more useful for difficult umbilical and incisional hernias than they are for large inguinal hernias. The critical surgeon recognizes that there is very little valid statistical evidence about the recurrence rates following different types of repair. The collection of truly comparable cases is not easy, and some of the methods used have not been tried for long enough to enable their true worth to be assessed. It is notable that much of the earlier enthusiasm for tantalum and stainless steel wire has died down owing to appreciation of the various difficulties already mentioned. The use of relatively rigid materials in the reinforcement of mobile structures introduces inevitable complications, and many surgeons (probably a growing number) are recognizing the virtues of repair with the patient's own tissues, provided this can be effected without tension. An understanding of the fundamentals of plastic surgery is certainly an advantage in planning the repair of large and difficult ruptures.

Nocturnal Priapism

Q.—*A healthy man of 56 complains that for over 20 years he has been troubled with a full penile erection every time he sleeps. It is not associated with erotic sensations or dreams of any kind. If he partially wakes, he is conscious of the condition and its discomfort, which does not alter unless he reaches a point of wakefulness that he describes as about half-way between sleep and full consciousness, when the erection immediately ceases. If he sleeps and wakes a number of times, the condition recurs each time. Is there any special significance in his complaint? I can find no cause.*

A.—These cases of nocturnal priapism in an elderly or middle-aged man are exceedingly puzzling. In only a few cases does one find any physical explanation, such as an irritative lesion of the posterior urethra or an enlarged prostate. Sometimes, but not often, there is a psychological explanation, but as nothing has been said in this case to indicate that the patient is suffering from a thwarted sex life, I assume a psychological factor does not explain it.

To sum up, therefore, it is quite usual to find no explanation in these cases. They begin mysteriously and end mysteriously.

Nutrient Enemas

Q.—*Are nutrient enemas—e.g., 5% dextrose—properly absorbed?*

A.—A solution of 5% dextrose is absorbed when given rectally. The colon, however, can absorb only 1 to 2 litres of fluid daily, so that a total of 75 g. (300 calories) glucose is the maximum that can be administered by this route. There can be few circumstances when it is not preferable to give glucose intravenously, as there is then no doubt about the degree and speed of its absorption. Proteins, peptones, and fats are not absorbed by the colon, and their administration by this route is not only useless but may be harmful, as the putrefactive bacteria break down those substances and form toxic products which may be absorbed.

Correction.—The authors of the article "Cortisone and A.C.T.H. in Treatment of Non-rheumatic Conditions" (*Journal*, January 2, p. 1) regret the omission of acknowledgments to Professor R. E. Tunbridge for access to the case records of two cases of Simmonds's disease and one of adrenal virilism.

"Any Questions?" Book.—The second book of selected Any Questions? is available, price 7s. 6d. (postage 6d.). Copies may be obtained either direct from the Publishing Manager, B.M.A. House, Tavistock Square, London, W.C.1, or from booksellers.

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